

Search history

10/27/2006

=> d his full

(FILE 'HOME' ENTERED AT 12:40:28 ON 26 OCT 2006)

FILE 'CAPLUS' ENTERED AT 12:40:34 ON 26 OCT 2006

E US2005-526780/APPS

L1 1 SEA ABB=ON PLU=ON US2005-526780/AP
D SCA
SEL RN

FILE 'REGISTRY' ENTERED AT 12:41:00 ON 26 OCT 2006

L2 9 SEA ABB=ON PLU=ON (24201-13-6/BI OR 33996-28-0/BI OR
33996-30-4/BI OR 672285-79-9/BI OR 672285-80-2/BI OR 672285-81-
3/BI OR 672285-82-4/BI OR 672285-83-5/BI OR 672285-84-6/BI)
D SCA

FILE 'STNGUIDE' ENTERED AT 12:44:26 ON 26 OCT 2006

FILE 'REGISTRY' ENTERED AT 12:53:56 ON 26 OCT 2006

L3 STRUCTURE UPLOADED

L4 4 SEA SSS SAM L3

D SCA

L5 STRUCTURE UPLOADED

L6 4 SEA SSS SAM L5

L7 47 SEA SSS FUL L5

SAVE TEMP L7 SPI780STR7L/A

FILE 'CAPLUS' ENTERED AT 12:59:24 ON 26 OCT 2006

L8 18 SEA ABB=ON PLU=ON L7

L9 1 SEA ABB=ON PLU=ON L8 AND L1

D SCA

SEL HIT RN

FILE 'REGISTRY' ENTERED AT 13:01:16 ON 26 OCT 2006

L10 2 SEA ABB=ON PLU=ON (672285-79-9/BI OR 672285-84-6/BI)

FILE 'REGISTRY' ENTERED AT 13:01:41 ON 26 OCT 2006

D IDE L10 1-2

FILE 'CAPLUS' ENTERED AT 13:03:06 ON 26 OCT 2006

D SCA L8

L11 105205 SEA ABB=ON PLU=ON ?STOMACH?/BI

L12 42051 SEA ABB=ON PLU=ON ?MOTIL?/BI

L13 4188 SEA ABB=ON PLU=ON ?PERISTAL?/BI

L14 249583 SEA ABB=ON PLU=ON ?DIGEST?/BI

L*** DEL 199220 S ?INTESTIN?

L15 288318 SEA ABB=ON PLU=ON ?INTESTIN?/BI

L16 43191 SEA ABB=ON PLU=ON (5HT OR 5 HT?)/BI

L17 77545 SEA ABB=ON PLU=ON ?SEROTONIN?/BI

L18 22550 SEA ABB=ON PLU=ON ?ILEUM?/BI

L19 18576 SEA ABB=ON PLU=ON ?JEJUN?/BI

L20 31539 SEA ABB=ON PLU=ON ?DUODEN?/BI

L21 139482 SEA ABB=ON PLU=ON TRACT#/BI

L22 171670 SEA ABB=ON PLU=ON ?GASTR?/BI

L23 12 SEA ABB=ON PLU=ON L8 AND (L11 OR L12 OR L13 OR L14 OR L15 OR
L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22)

L24 162 SEA ABB=ON PLU=ON KITAJIMA A?/AU

L25 3 SEA ABB=ON PLU=ON AKIHIKO K?/AU

L26 5 SEA ABB=ON PLU=ON KAMODA O?/AU

L27 22 SEA ABB=ON PLU=ON OSAMU K?/AU

E KAMODA/AU

L28 6 SEA ABB=ON PLU=ON OHSAKO A?/AU
 L29 2 SEA ABB=ON PLU=ON AKIHIRO O?/AU
 L30 574 SEA ABB=ON PLU=ON YANAGI T?/AU
 L31 1 SEA ABB=ON PLU=ON TOSHIHARU Y?/AU
 L32 165 SEA ABB=ON PLU=ON (L24 OR L25)
 L33 27 SEA ABB=ON PLU=ON (L26 OR L27)
 L34 8 SEA ABB=ON PLU=ON (L28 OR L29)
 L35 575 SEA ABB=ON PLU=ON (L30 OR L31)
 L36 1 SEA ABB=ON PLU=ON L32 AND (L33 OR L34 OR L35)
 L37 5 SEA ABB=ON PLU=ON L33 AND (L34 OR L35)
 L38 1 SEA ABB=ON PLU=ON L34 AND L35
 L39 5 SEA ABB=ON PLU=ON (L36 OR L37 OR L38)
 L40 3 SEA ABB=ON PLU=ON (L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR
 L30 OR L31) AND (L23 OR L8)

FILE 'MEDLINE' ENTERED AT 13:14:46 ON 26 OCT 2006

L41 235 SEA ABB=ON PLU=ON (L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR
 L30 OR L31)
 L42 2 SEA ABB=ON PLU=ON (L36 OR L37 OR L38)

FILE 'REGISTRY' ENTERED AT 13:16:02 ON 26 OCT 2006

L43 SET SMARTSELECT ON
 SEL PLU=ON L7 1- CHEM : 49 TERMS
 SET SMARTSELECT OFF

FILE 'MEDLINE' ENTERED AT 13:16:05 ON 26 OCT 2006

L44 3 SEA ABB=ON PLU=ON L43
 D SCA
 D TRIAL 1-3
 D QUE L44
 D L43
 D L43 1-49
 L45 0 SEA ABB=ON PLU=ON FAUC65
 L46 5 SEA ABB=ON PLU=ON TKS159
 D TRIAL 1-5
 L47 1149902 SEA ABB=ON PLU=ON (L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR
 L17 OR L18 OR L19 OR L20 OR L21 OR L22)
 L48 5 SEA ABB=ON PLU=ON L47 AND ((L44 OR L45 OR L46))
 L49 2 SEA ABB=ON PLU=ON L41 AND (L44 OR L46 OR L48)

FILE 'EMBASE' ENTERED AT 13:20:17 ON 26 OCT 2006

L50 198 SEA ABB=ON PLU=ON (L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR
 L30 OR L31)
 L51 2 SEA ABB=ON PLU=ON (L36 OR L37 OR L38)

FILE 'REGISTRY' ENTERED AT 13:20:54 ON 26 OCT 2006

L52 SET SMARTSELECT ON
 SEL PLU=ON L7 1- CHEM : 49 TERMS
 SET SMARTSELECT OFF

FILE 'EMBASE' ENTERED AT 13:20:56 ON 26 OCT 2006

L53 7 SEA ABB=ON PLU=ON L52
 L54 4 SEA ABB=ON PLU=ON FAUC65 OR TKS159
 L55 7 SEA ABB=ON PLU=ON (L53 OR L54)
 L56 7 SEA ABB=ON PLU=ON (L53 OR L54) AND (L11 OR L12 OR L13 OR L14
 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22).
 D TRIAL 1-7
 L57 2 SEA ABB=ON PLU=ON L50 AND (L53 OR L54 OR L56)

FILE 'BIOSIS' ENTERED AT 13:25:28 ON 26 OCT 2006
 L58 252 SEA ABB=ON PLU=ON (L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR
 L30 OR L31)
 L59 4 SEA ABB=ON PLU=ON (L36 OR L37 OR L38)

FILE 'REGISTRY' ENTERED AT 13:25:56 ON 26 OCT 2006
 L60 SET SMARTSELECT ON
 SEL PLU=ON L7 1- CHEM : 49 TERMS
 SET SMARTSELECT OFF

FILE 'BIOSIS' ENTERED AT 13:25:57 ON 26 OCT 2006
 L61 3 SEA ABB=ON PLU=ON L60
 L62 5 SEA ABB=ON PLU=ON FAUC65 OR TKS159
 L63 2 SEA ABB=ON PLU=ON L58 AND (L61 OR L62)

FILE 'REGISTRY' ENTERED AT 13:27:39 ON 26 OCT 2006
 L64 1 SEA ABB=ON PLU=ON FAUC 65/CN
 L65 1 SEA ABB=ON PLU=ON TKS 159/CN
 D SCA
 D SCA L64
 SEL RN L10
 SEL RN L64
 SEL RN L65
 L66 1 SEA ABB=ON PLU=ON (672285-79-9/CRN OR 672285-84-6/CRN OR
 627529-76-4/CRN OR 142228-17-9/CRN)
 D SCA
 D IDE L64
 D IDE L65
 D IDE L66
 D STAT QUE L7
 L67 4 SEA ABB=ON PLU=ON L65 OR L66 OR L10
 D SCA

FILE 'USPATFULL, USPAT2' ENTERED AT 13:39:42 ON 26 OCT 2006
 L68 3 SEA ABB=ON PLU=ON L67
 D SCA
 L69 4 SEA ABB=ON PLU=ON L7
 L70 308291 SEA ABB=ON PLU=ON (L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR
 L17 OR L18 OR L19 OR L20 OR L21 OR L22)
 L71 3 SEA ABB=ON PLU=ON L69 AND L70
 L72 183 SEA ABB=ON PLU=ON L41
 L73 7 SEA ABB=ON PLU=ON L42
 L74 1 SEA ABB=ON PLU=ON L72 AND (L69 OR L71)

FILE 'STNGUIDE' ENTERED AT 13:42:37 ON 26 OCT 2006

FILE 'REGISTRY' ENTERED AT 13:45:53 ON 26 OCT 2006
 D STAT QUE L7

FILE 'CAPLUS' ENTERED AT 13:45:54 ON 26 OCT 2006
 D QUE NOS L39
 D QUE NOS L40
 L75 6 SEA ABB=ON PLU=ON L39 OR L40

FILE 'MEDLINE' ENTERED AT 13:45:58 ON 26 OCT 2006
 D QUE NOS L42
 D QUE NOS L49
 L76 3 SEA ABB=ON PLU=ON L42 OR L49

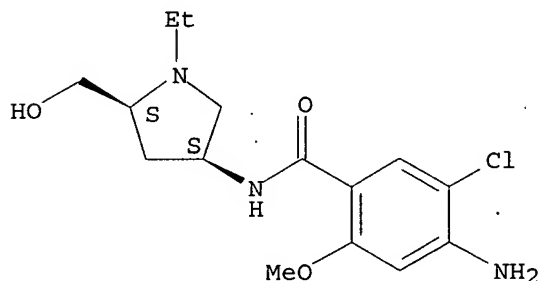
FILE 'EMBASE' ENTERED AT 13:46:01 ON 26 OCT 2006

12 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d ide L66

L66 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
 RN 142347-77-1 REGISTRY
 ED Entered STN: 10 Jul 1992
 CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride, (3S-cis)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C15 H22 Cl N3 O3 . Cl H
 SR CA
 LC STN Files: CA, CAPLUS, PROUSDDR, USPATFULL
 CRN (142228-17-9)

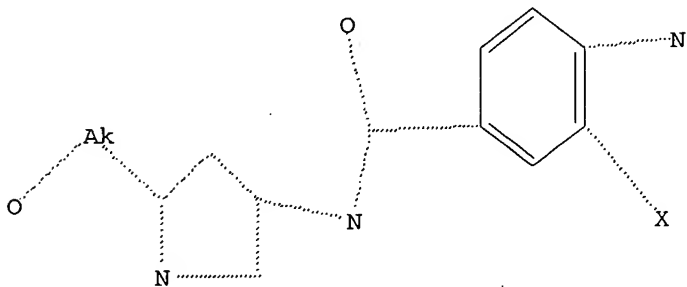
Absolute stereochemistry.



● HCl

2 REFERENCES IN FILE CA (1907 TO DATE)
 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> => d stat que L7
 L5 STR



Structure attributes must be viewed using STN Express query preparation.
 L7 47 SEA FILE=REGISTRY SSS FUL L5

100.0% PROCESSED 11082 ITERATIONS
 SEARCH TIME: 00.00.01

47 ANSWERS

=> => file registry

FILE 'REGISTRY' ENTERED AT 13:45:53 ON 26 OCT 2006

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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STRUCTURE FILE UPDATES: 25 OCT 2006 HIGHEST RN 911284-77-0

DICTIONARY FILE UPDATES: 25 OCT 2006 HIGHEST RN 911284-77-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

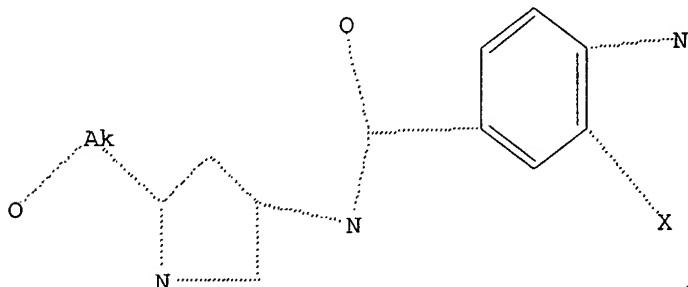
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

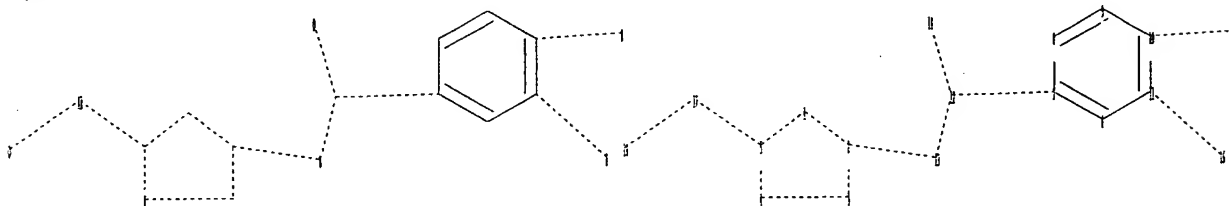
=> d stat que L7

L5

STR



Structure attributes must be viewed using STN Express query preparation.
Uploading L5.str



chain nodes :

12 13 14 15 16 17 18

ring nodes :

1 2 3 4 5 6 7 8 9 10 11

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
See also:

<http://www.nlm.nih.gov/mesh/>
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE EMBASE

FILE COVERS 1974 TO 26 Oct 2006 (20061026/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS

FILE COVERS 1969 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 18 October 2006 (20061018/ED)

FILE USPATFULL

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 26 Oct 2006 (20061026/PD)

FILE LAST UPDATED: 26 Oct 2006 (20061026/ED)

HIGHEST GRANTED PATENT NUMBER: US7127745

HIGHEST APPLICATION PUBLICATION NUMBER: US2006242744

CA INDEXING IS CURRENT THROUGH 24 Oct 2006 (20061024/UPCA)

ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 26 Oct 2006 (20061026/PD)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2006

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2006

FILE USPAT2

FILE COVERS 2001 TO PUBLICATION DATE: 26 Oct 2006 (20061026/PD)

FILE LAST UPDATED: 26 Oct 2006 (20061026/ED)

HIGHEST GRANTED PATENT NUMBER: US2006139723

HIGHEST APPLICATION PUBLICATION NUMBER: US2006242346

CA INDEXING IS CURRENT THROUGH 26 Oct 2006 (20061026/UPCA)

ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 26 Oct 2006 (20061026/PD)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2006

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2006

10/27/2006

=> file registry

FILE 'REGISTRY' ENTERED AT 13:01:41 ON 26 OCT 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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STRUCTURE FILE UPDATES: 25 OCT 2006 HIGHEST RN 911284-77-0
DICTIONARY FILE UPDATES: 25 OCT 2006 HIGHEST RN 911284-77-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

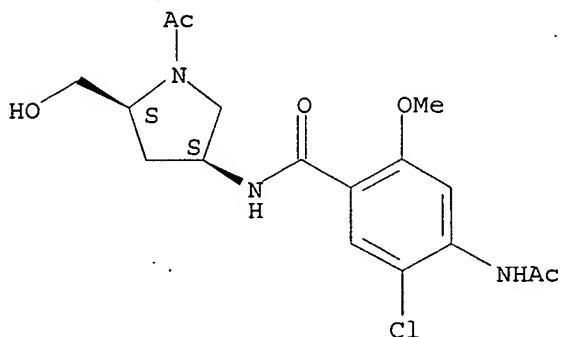
REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=> d ide L10 1-2

L10 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN
RN 672285-84-6 REGISTRY
ED Entered STN: 07 Apr 2004
CN Benzamide, 4-(acetylamino)-N-[(3S,5S)-1-acetyl-5-(hydroxymethyl)-3-
pyrrolidiny]-5-chloro-2-methoxy- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C17 H22 Cl N3 O5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



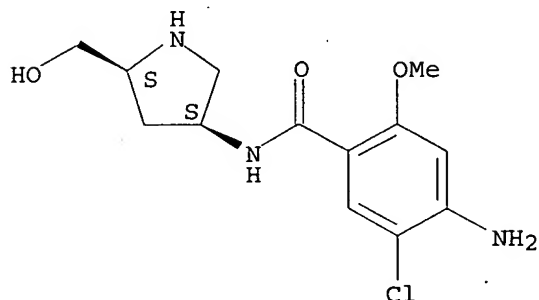
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

10/27/2006

L10 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN
RN 672285-79-9 REGISTRY
ED Entered STN: 07 Apr 2004
CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C13 H18 Cl N3 O3 . Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
CRN (765269-94-1)

Absolute stereochemistry.



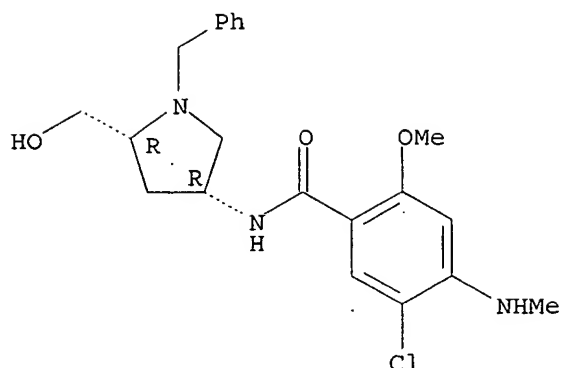
● HCl

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> => => d ide L64

L64 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN 627529-76-4 REGISTRY
ED Entered STN: 19 Dec 2003
CN Benzamide, 5-chloro-N-[(3R,5R)-5-(hydroxymethyl)-1-(phenylmethyl)-3-pyrrolidinyl]-2-methoxy-4-(methylamino)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN FAUC 65
FS STEREOSEARCH
MF C21 H26 Cl N3 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d ide L65

L65 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN

RN 142228-17-9 REGISTRY

ED Entered STN: 03 Jul 1992

CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, (3S-cis)-

OTHER NAMES:

CN **TKS 159**

FS STEREOSEARCH

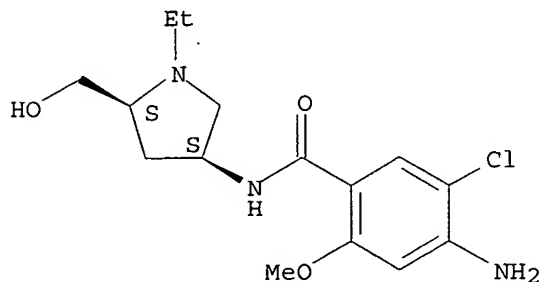
MF C15 H22 Cl N3 O3

CI COM

SR CA

LC STN Files: ADISINSIGHT, BIOSIS, CA, CAPLUS, PROUSDDR, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

12 REFERENCES IN FILE CA (1907 TO DATE)

D QUE NOS L51
 D QUE NOS L57
 L77 3 SEA ABB=ON PLU=ON L51 OR L57

 FILE 'BIOSIS' ENTERED AT 13:46:04 ON 26 OCT 2006
 D QUE NOS L59
 D QUE NOS L63
 L78 5 SEA ABB=ON PLU=ON L59 OR L63

 FILE 'USPATFULL, USPAT2' ENTERED AT 13:46:07 ON 26 OCT 2006
 D QUE NOS L73
 D QUE NOS L74
 L79 7 SEA ABB=ON PLU=ON L73 OR L74

 FILE 'STNGUIDE' ENTERED AT 13:46:29 ON 26 OCT 2006

 FILE 'CAPLUS, MEDLINE, EMBASE, BIOSIS, USPATFULL, USPAT2' ENTERED AT
 13:46:50 ON 26 OCT 2006
 L80 12 DUP REM L75 L76 L77 L78 L79 (12 DUPLICATES REMOVED)
 ANSWERS '1-6' FROM FILE CAPLUS
 ANSWERS '7-9' FROM FILE BIOSIS
 ANSWERS '10-12' FROM FILE USPATFULL
 D IBIB ABS HITIND HITSTR L80 1-6
 D IALL L80 7-9
 D IBIB ABS KWIC HITSTR L80 10-12

 FILE 'REGISTRY' ENTERED AT 13:51:05 ON 26 OCT 2006
 D STAT QUE L7

 FILE 'CAPLUS' ENTERED AT 13:51:07 ON 26 OCT 2006
 D QUE NOS L8
 D QUE NOS L23
 L81 15 SEA ABB=ON PLU=ON (L8 OR L23) NOT L75

 FILE 'MEDLINE' ENTERED AT 13:51:10 ON 26 OCT 2006
 D QUE NOS L44
 D QUE NOS L46
 D QUE NOS L48
 L82 3 SEA ABB=ON PLU=ON (L44 OR L46 OR L48) NOT L76

 FILE 'EMBASE' ENTERED AT 13:51:14 ON 26 OCT 2006
 D QUE NOS L53
 D QUE NOS L54
 D QUE NOS L56
 L83 5 SEA ABB=ON PLU=ON (L53 OR L54 OR L56) NOT L77

 FILE 'BIOSIS' ENTERED AT 13:51:18 ON 26 OCT 2006
 D QUE NOS L61
 D QUE NOS L62
 L84 3 SEA ABB=ON PLU=ON (L61 OR L62) NOT L78

 FILE 'USPATFULL, USPAT2' ENTERED AT 13:51:21 ON 26 OCT 2006
 D QUE NOS L69
 D QUE NOS L71
 L85 3 SEA ABB=ON PLU=ON (L69 OR L71) NOT L79

 FILE 'CAPLUS, MEDLINE, EMBASE, BIOSIS, USPATFULL' ENTERED AT 13:53:56 ON
 26 OCT 2006
 L86 22 DUP REM L81 L82 L83 L84 L85 (7 DUPLICATES REMOVED)
 ANSWERS '1-15' FROM FILE CAPLUS

=> => file registry

FILE 'REGISTRY' ENTERED AT 13:45:53 ON 26 OCT 2006

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STRUCTURE FILE UPDATES: 25 OCT 2006 HIGHEST RN 911284-77-0

DICTIONARY FILE UPDATES: 25 OCT 2006 HIGHEST RN 911284-77-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

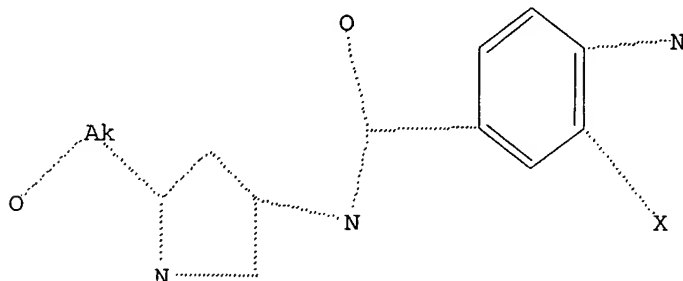
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

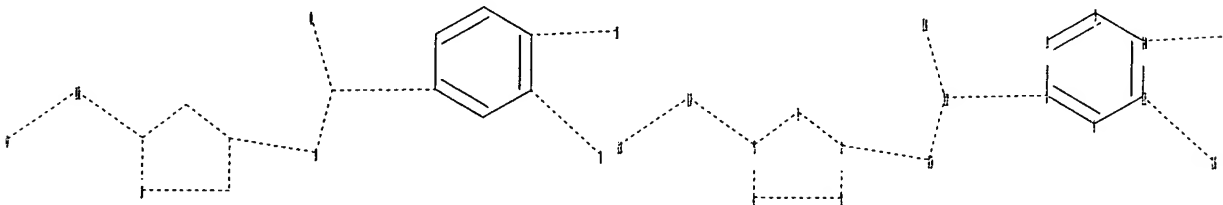
=> d stat que L7

L5

STR



Structure attributes must be viewed using STN Express query preparation.
Uploading L5.str



chain nodes :

12 13 14 15 16 17 18

ring nodes :

1 2 3 4 5 6 7 8 9 10 11

chain bonds :
 2-13 5-17 7-12 10-15 11-16 12-13 12-14 17-18
 ring bonds :
 1-2 1-5 2-3 3-4 4-5 6-7 6-11 7-8 8-9 9-10 10-11
 exact/norm bonds :
 1-2 1-5 2-3 2-13 3-4 4-5 5-17 7-12 10-15 11-16 12-13 12-14 17-18
 normalized bonds :
 6-7 6-11 7-8 8-9 9-10 10-11

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
 11:Atom 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS

L7 47 SEA FILE=REGISTRY SSS FUL L5

100.0% PROCESSED 11082 ITERATIONS
 SEARCH TIME: 00.00.01

47 ANSWERS

=> file caplus

FILE 'CAPLUS' ENTERED AT 13:45:54 ON 26 OCT 2006
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AUTHOR
 SEARCH

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FILE COVERS 1907 - 26 Oct 2006 VOL 145 ISS 18
 FILE LAST UPDATED: 25 Oct 2006 (20061025/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>
 'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d que nos L39

L24	162	SEA FILE=CAPLUS	ABB=ON	PLU=ON	KITAJIMA A?/AU
L25	3	SEA FILE=CAPLUS	ABB=ON	PLU=ON	AKIHIKO K?/AU
L26	5	SEA FILE=CAPLUS	ABB=ON	PLU=ON	KAMODA O?/AU
L27	22	SEA FILE=CAPLUS	ABB=ON	PLU=ON	OSAMU K?/AU
L28	6	SEA FILE=CAPLUS	ABB=ON	PLU=ON	OHSAKO A?/AU
L29	2	SEA FILE=CAPLUS	ABB=ON	PLU=ON	AKIHIRO O?/AU
L30	574	SEA FILE=CAPLUS	ABB=ON	PLU=ON	YANAGI T?/AU


```

L31      1 SEA FILE=CAPLUS ABB=ON PLU=ON TOSHIHARU Y?/AU
L32     165 SEA FILE=CAPLUS ABB=ON PLU=ON (L24 OR L25)
L33      27 SEA FILE=CAPLUS ABB=ON PLU=ON (L26 OR L27)
L34       8 SEA FILE=CAPLUS ABB=ON PLU=ON (L28 OR L29)
L35     575 SEA FILE=CAPLUS ABB=ON PLU=ON (L30 OR L31)
L36       1 SEA FILE=CAPLUS ABB=ON PLU=ON L32 AND (L33 OR L34 OR L35)
L37       5 SEA FILE=CAPLUS ABB=ON PLU=ON L33 AND (L34 OR L35)
L38       1 SEA FILE=CAPLUS ABB=ON PLU=ON L34 AND L35
L39       5 SEA FILE=CAPLUS ABB=ON PLU=ON (L36 OR L37 OR L38)

```

=> d que nos L40

```

L5        STR
L7        47 SEA FILE=REGISTRY SSS FUL L5
L8        18 SEA FILE=CAPLUS ABB=ON PLU=ON L7
L11     105205 SEA FILE=CAPLUS ABB=ON PLU=ON ?STOMACH?/BI
L12     42051 SEA FILE=CAPLUS ABB=ON PLU=ON ?MOTIL?/BI
L13     4188 SEA FILE=CAPLUS ABB=ON PLU=ON ?PERISTAL?/BI
L14     249583 SEA FILE=CAPLUS ABB=ON PLU=ON ?DIGEST?/BI
L15     288318 SEA FILE=CAPLUS ABB=ON PLU=ON ?INTESTIN?/BI
L16     43191 SEA FILE=CAPLUS ABB=ON PLU=ON (5HT OR 5 HT?)/BI
L17     77545 SEA FILE=CAPLUS ABB=ON PLU=ON ?SEROTONIN?/BI
L18     22550 SEA FILE=CAPLUS ABB=ON PLU=ON ?ILEUM?/BI
L19     18576 SEA FILE=CAPLUS ABB=ON PLU=ON ?JEJUN?/BI
L20     31539 SEA FILE=CAPLUS ABB=ON PLU=ON ?DUODEN?/BI
L21     139482 SEA FILE=CAPLUS ABB=ON PLU=ON TRACT#/BI
L22     171670 SEA FILE=CAPLUS ABB=ON PLU=ON ?GASTR?/BI
L23       12 SEA FILE=CAPLUS ABB=ON PLU=ON L8 AND (L11 OR L12 OR L13 OR
L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22)
L24     162 SEA FILE=CAPLUS ABB=ON PLU=ON KITAJIMA A?/AU
L25       3 SEA FILE=CAPLUS ABB=ON PLU=ON AKIHIKO K?/AU
L26       5 SEA FILE=CAPLUS ABB=ON PLU=ON KAMODA O?/AU
L27     22 SEA FILE=CAPLUS ABB=ON PLU=ON OSAMU K?/AU
L28       6 SEA FILE=CAPLUS ABB=ON PLU=ON OHSAKO A?/AU
L29       2 SEA FILE=CAPLUS ABB=ON PLU=ON AKIHIRO O?/AU
L30     574 SEA FILE=CAPLUS ABB=ON PLU=ON YANAGI T?/AU
L31       1 SEA FILE=CAPLUS ABB=ON PLU=ON TOSHIHARU Y?/AU
L40       3 SEA FILE=CAPLUS ABB=ON PLU=ON (L24 OR L25 OR L26 OR L27 OR
L28 OR L29 OR L30 OR L31) AND (L23 OR L8)

```

=> s L39 or L40

L75 6 L39 OR L40

=> file medline

FILE 'MEDLINE' ENTERED AT 13:45:58 ON 26 OCT 2006

FILE LAST UPDATED: 25 Oct 2006 (20061025/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).

See also:

<http://www.nlm.nih.gov/mesh/>
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que nos L42

L24	162	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	KITAJIMA A?/AU
L25	3	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	AKIHIKO K?/AU
L26	5	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	KAMODA O?/AU
L27	22	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	OSAMU K?/AU
L28	6	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	OHSAKO A?/AU
L29	2	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	AKIHIRO O?/AU
L30	574	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	YANAGI T?/AU
L31	1	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	TOSHIHARU Y?/AU
L32	165	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	(L24 OR L25)
L33	27	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	(L26 OR L27)
L34	8	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	(L28 OR L29)
L35	575	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	(L30 OR L31)
L36	1	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	L32 AND (L33 OR L34 OR L35)
L37	5	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	L33 AND (L34 OR L35)
L38	1	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	L34 AND L35
L42	2	SEA	FILE=MEDLINE	ABB=ON	PLU=ON	(L36 OR L37 OR L38)

=> d que nos L49

L5		STR				
L7	47	SEA	FILE=REGISTRY	SSS	FUL	L5
L11	105205	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	?STOMACH?/BI
L12	42051	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	?MOTIL?/BI
L13	4188	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	?PERISTAL?/BI
L14	249583	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	?DIGEST?/BI
L15	288318	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	?INTESTIN?/BI
L16	43191	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	(5HT OR 5 HT?)/BI
L17	77545	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	?SEROTONIN?/BI
L18	22550	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	?ILEUM?/BI
L19	18576	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	?JEJUN?/BI
L20	31539	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	?DUODEN?/BI
L21	139482	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	TRACT#/BI
L22	171670	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	?GASTR?/BI
L24	162	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	KITAJIMA A?/AU
L25	3	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	AKIHIKO K?/AU
L26	5	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	KAMODA O?/AU
L27	22	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	OSAMU K?/AU
L28	6	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	OHSAKO A?/AU
L29	2	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	AKIHIRO O?/AU
L30	574	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	YANAGI T?/AU
L31	1	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	TOSHIHARU Y?/AU
L41	235	SEA	FILE=MEDLINE	ABB=ON	PLU=ON	(L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31)
L43		SEL	PLU=ON	L7 1- CHEM :		49 TERMS
L44	3	SEA	FILE=MEDLINE	ABB=ON	PLU=ON	L43
L45	0	SEA	FILE=MEDLINE	ABB=ON	PLU=ON	FAUC65

```

L46          5 SEA FILE=MEDLINE ABB=ON  PLU=ON  TKS159
L47      1149902 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L11 OR L12 OR L13 OR L14 OR
              L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22)
L48          5 SEA FILE=MEDLINE ABB=ON  PLU=ON  L47 AND ((L44 OR L45 OR L46))
L49          2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L41 AND (L44 OR L46 OR L48)

```

=> s L42 or L49

L76 3 L42 OR L49

=> file embase

FILE 'EMBASE' ENTERED AT 13:46:01 ON 26 OCT 2006
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FILE COVERS 1974 TO 26 Oct 2006 (20061026/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default)
 and biweekly.

This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que nos L51

```

L24          162 SEA FILE=CAPLUS ABB=ON  PLU=ON  KITAJIMA A?/AU
L25           3 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIKO K?/AU
L26           5 SEA FILE=CAPLUS ABB=ON  PLU=ON  KAMODA O?/AU
L27          22 SEA FILE=CAPLUS ABB=ON  PLU=ON  OSAMU K?/AU
L28           6 SEA FILE=CAPLUS ABB=ON  PLU=ON  OHSAKO A?/AU
L29           2 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIRO O?/AU
L30          574 SEA FILE=CAPLUS ABB=ON  PLU=ON  YANAGI T?/AU
L31           1 SEA FILE=CAPLUS ABB=ON  PLU=ON  TOSHIHARU Y?/AU
L32          165 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L24 OR L25)
L33           27 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L26 OR L27)
L34           8 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L28 OR L29)
L35          575 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L30 OR L31)
L36           1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L32 AND (L33 OR L34 OR L35)
L37           5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L33 AND (L34 OR L35)
L38           1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L34 AND L35
L51           2 SEA FILE=EMBASE ABB=ON  PLU=ON  (L36 OR L37 OR L38)

```

=> d que nos L57

```

L5           STR
L7           47 SEA FILE=REGISTRY SSS FUL L5
L11          105205 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?STOMACH?/BI
L12           42051 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?MOTIL?/BI
L13           4188 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?PERISTAL?/BI
L14          249583 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?DIGEST?/BI
L15          288318 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?INTESTIN?/BI
L16           43191 SEA FILE=CAPLUS ABB=ON  PLU=ON  (5HT OR 5 HT?)/BI
L17           77545 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?SEROTONIN?/BI
L18           22550 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?ILEUM?/BI
L19           18576 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?JEJUN?/BI

```

```

L20      31539 SEA FILE=CAPLUS ABB=ON PLU=ON ?DUODEN?/BI
L21      139482 SEA FILE=CAPLUS ABB=ON PLU=ON TRACT#/BI
L22      171670 SEA FILE=CAPLUS ABB=ON PLU=ON ?GASTR?/BI
L24      162 SEA FILE=CAPLUS ABB=ON PLU=ON KITAJIMA A?/AU
L25      3 SEA FILE=CAPLUS ABB=ON PLU=ON AKIHIKO K?/AU
L26      5 SEA FILE=CAPLUS ABB=ON PLU=ON KAMODA O?/AU
L27      22 SEA FILE=CAPLUS ABB=ON PLU=ON OSAMU K?/AU
L28      6 SEA FILE=CAPLUS ABB=ON PLU=ON OHSAKO A?/AU
L29      2 SEA FILE=CAPLUS ABB=ON PLU=ON AKIHIRO O?/AU
L30      574 SEA FILE=CAPLUS ABB=ON PLU=ON YANAGI T?/AU
L31      1 SEA FILE=CAPLUS ABB=ON PLU=ON TOSHIHARU Y?/AU
L50      198 SEA FILE=EMBASE ABB=ON PLU=ON (L24 OR L25 OR L26 OR L27 OR
      L28 OR L29 OR L30 OR L31)
L52      SEL PLU=ON L7 1- CHEM : 49 TERMS
L53      7 SEA FILE=EMBASE ABB=ON PLU=ON L52
L54      4 SEA FILE=EMBASE ABB=ON PLU=ON FAUC65 OR TKS159
L56      7 SEA FILE=EMBASE ABB=ON PLU=ON (L53 OR L54) AND (L11 OR L12
      OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21
      OR L22)
L57      2 SEA FILE=EMBASE ABB=ON PLU=ON L50 AND (L53 OR L54 OR L56)

```

=> s L51 or L57

L77 3 L51 OR L57

=> file biosis

FILE 'BIOSIS' ENTERED AT 13:46:04 ON 26 OCT 2006
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 18 October 2006 (20061018/ED)

=> d que nos L59

```

L24      162 SEA FILE=CAPLUS ABB=ON PLU=ON KITAJIMA A?/AU
L25      3 SEA FILE=CAPLUS ABB=ON PLU=ON AKIHIKO K?/AU
L26      5 SEA FILE=CAPLUS ABB=ON PLU=ON KAMODA O?/AU
L27      22 SEA FILE=CAPLUS ABB=ON PLU=ON OSAMU K?/AU
L28      6 SEA FILE=CAPLUS ABB=ON PLU=ON OHSAKO A?/AU
L29      2 SEA FILE=CAPLUS ABB=ON PLU=ON AKIHIRO O?/AU
L30      574 SEA FILE=CAPLUS ABB=ON PLU=ON YANAGI T?/AU
L31      1 SEA FILE=CAPLUS ABB=ON PLU=ON TOSHIHARU Y?/AU
L32      165 SEA FILE=CAPLUS ABB=ON PLU=ON (L24 OR L25)
L33      27 SEA FILE=CAPLUS ABB=ON PLU=ON (L26 OR L27)
L34      8 SEA FILE=CAPLUS ABB=ON PLU=ON (L28 OR L29)
L35      575 SEA FILE=CAPLUS ABB=ON PLU=ON (L30 OR L31)
L36      1 SEA FILE=CAPLUS ABB=ON PLU=ON L32 AND (L33 OR L34 OR L35).
L37      5 SEA FILE=CAPLUS ABB=ON PLU=ON L33 AND (L34 OR L35)
L38      1 SEA FILE=CAPLUS ABB=ON PLU=ON L34 AND L35
L59      4 SEA FILE=BIOSIS ABB=ON PLU=ON (L36 OR L37 OR L38)

```

=> d que nos L63

```

L5          STR
L7          47 SEA FILE=REGISTRY SSS FUL L5
L24         162 SEA FILE=CAPLUS ABB=ON   PLU=ON   KITAJIMA A?/AU
L25         3 SEA FILE=CAPLUS ABB=ON   PLU=ON   AKIHIKO K?/AU
L26         5 SEA FILE=CAPLUS ABB=ON   PLU=ON   KAMODA O?/AU
L27         22 SEA FILE=CAPLUS ABB=ON   PLU=ON   OSAMU K?/AU
L28         6 SEA FILE=CAPLUS ABB=ON   PLU=ON   OHSAKO A?/AU
L29         2 SEA FILE=CAPLUS ABB=ON   PLU=ON   AKIHIRO O?/AU
L30         574 SEA FILE=CAPLUS ABB=ON   PLU=ON   YANAGI T?/AU
L31         1 SEA FILE=CAPLUS ABB=ON   PLU=ON   TOSHIHARU Y?/AU
L58         252 SEA FILE=BIOSIS ABB=ON   PLU=ON   (L24 OR L25 OR L26 OR L27 OR
          L28 OR L29 OR L30 OR L31)
L60         SEL PLU=ON L7 1- CHEM :      49 TERMS
L61         3 SEA FILE=BIOSIS ABB=ON   PLU=ON   L60
L62         5 SEA FILE=BIOSIS ABB=ON   PLU=ON   FAUC65 OR TKS159
L63         2 SEA FILE=BIOSIS ABB=ON   PLU=ON   L58 AND (L61 OR L62)

```

=> s L59 or L63

L78 5 L59 OR L63

=> file uspatall

FILE 'USPATFULL' ENTERED AT 13:46:07 ON 26 OCT 2006
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FILE 'USPAT2' ENTERED AT 13:46:07 ON 26 OCT 2006
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=> d que nos L73

```

L24         162 SEA FILE=CAPLUS ABB=ON   PLU=ON   KITAJIMA A?/AU
L25         3 SEA FILE=CAPLUS ABB=ON   PLU=ON   AKIHIKO K?/AU
L26         5 SEA FILE=CAPLUS ABB=ON   PLU=ON   KAMODA O?/AU
L27         22 SEA FILE=CAPLUS ABB=ON   PLU=ON   OSAMU K?/AU
L28         6 SEA FILE=CAPLUS ABB=ON   PLU=ON   OHSAKO A?/AU
L29         2 SEA FILE=CAPLUS ABB=ON   PLU=ON   AKIHIRO O?/AU
L30         574 SEA FILE=CAPLUS ABB=ON   PLU=ON   YANAGI T?/AU
L31         1 SEA FILE=CAPLUS ABB=ON   PLU=ON   TOSHIHARU Y?/AU
L32         165 SEA FILE=CAPLUS ABB=ON   PLU=ON   (L24 OR L25)
L33         27 SEA FILE=CAPLUS ABB=ON   PLU=ON   (L26 OR L27)
L34         8 SEA FILE=CAPLUS ABB=ON   PLU=ON   (L28 OR L29)
L35         575 SEA FILE=CAPLUS ABB=ON   PLU=ON   (L30 OR L31)
L36         1 SEA FILE=CAPLUS ABB=ON   PLU=ON   L32 AND (L33 OR L34 OR L35)
L37         5 SEA FILE=CAPLUS ABB=ON   PLU=ON   L33 AND (L34 OR L35)
L38         1 SEA FILE=CAPLUS ABB=ON   PLU=ON   L34 AND L35
L42         2 SEA FILE=MEDLINE ABB=ON   PLU=ON   (L36 OR L37 OR L38)
L73         7 SEA L42

```

=> d que nos L74

```

L5          STR
L7          47 SEA FILE=REGISTRY SSS FUL L5
L11         105205 SEA FILE=CAPLUS ABB=ON   PLU=ON   ?STOMACH?/BI
L12         42051 SEA FILE=CAPLUS ABB=ON   PLU=ON   ?MOTIL?/BI
L13         4188 SEA FILE=CAPLUS ABB=ON   PLU=ON   ?PERISTAL?/BI
L14         249583 SEA FILE=CAPLUS ABB=ON   PLU=ON   ?DIGEST?/BI
L15         288318 SEA FILE=CAPLUS ABB=ON   PLU=ON   ?INTESTIN?/BI

```

```

L16      43191 SEA FILE=CAPLUS ABB=ON PLU=ON (5HT OR 5 HT?)/BI
L17      77545 SEA FILE=CAPLUS ABB=ON PLU=ON ?SEROTONIN?/BI
L18      22550 SEA FILE=CAPLUS ABB=ON PLU=ON ?ILEUM?/BI
L19      18576 SEA FILE=CAPLUS ABB=ON PLU=ON ?JEJUN?/BI
L20      31539 SEA FILE=CAPLUS ABB=ON PLU=ON ?DUODEN?/BI
L21      139482 SEA FILE=CAPLUS ABB=ON PLU=ON TRACT#/BI
L22      171670 SEA FILE=CAPLUS ABB=ON PLU=ON ?GASTR?/BI
L24       162 SEA FILE=CAPLUS ABB=ON PLU=ON KITAJIMA A?/AU
L25       3 SEA FILE=CAPLUS ABB=ON PLU=ON AKIHIKO K?/AU
L26       5 SEA FILE=CAPLUS ABB=ON PLU=ON KAMODA O?/AU
L27      22 SEA FILE=CAPLUS ABB=ON PLU=ON OSAMU K?/AU
L28       6 SEA FILE=CAPLUS ABB=ON PLU=ON OHSAKO A?/AU
L29       2 SEA FILE=CAPLUS ABB=ON PLU=ON AKIHIRO O?/AU
L30      574 SEA FILE=CAPLUS ABB=ON PLU=ON YANAGI T?/AU
L31       1 SEA FILE=CAPLUS ABB=ON PLU=ON TOSHIHARU Y?/AU
L41      235 SEA FILE=MEDLINE ABB=ON PLU=ON (L24 OR L25 OR L26 OR L27 OR
      L28 OR L29 OR L30 OR L31)
L69       4 SEA L7
L70      308291 SEA (L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR
      L19 OR L20 OR L21 OR L22)
L71       3 SEA L69 AND L70
L72      183 SEA L41
L74       1 SEA L72 AND (L69 OR L71)

```

=> s L73 or L74

L79 7 L73 OR L74

=> => dup rem L75 L76 L77 L78 L79

FILE 'CAPLUS' ENTERED AT 13:46:50 ON 26 OCT 2006

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PROCESSING COMPLETED FOR L75

PROCESSING COMPLETED FOR L76

PROCESSING COMPLETED FOR L77

PROCESSING COMPLETED FOR L78

PROCESSING COMPLETED FOR L79

L80 12 DUP REM L75 L76 L77 L78 L79 (12 DUPLICATES REMOVED)

ANSWERS '1-6' FROM FILE CAPLUS

ANSWERS '7-9' FROM FILE BIOSIS

ANSWERS '10-12' FROM FILE USPATFULL

=> d ibib abs hitind hitstr L80 1-6; d iall L80 7-9; d ibib abs kwic hitstr L80 10-12

L80 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2006:953499 CAPLUS
 TITLE: In vitro activity of a novel antimicrobial agent, TG44, for treatment of Helicobacter pylori infection
 AUTHOR(S): Kamoda, Osamu; Anzai, Kinsei; Mizoguchi, Jun-ichi; Shiojiri, Masatoshi; Yanagi, Toshiharu; Nishino, Takeshi; Kamiya, Shigeru
 CORPORATE SOURCE: Quality Assurance Division, Nagase Chemtex Corporation, 1-58-1, Osadano-cho, Fukuchiyama, Kyoto, 620-0853, Japan
 SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(9), 3062-3069
 CODEN: AMACCQ; ISSN: 0066-4804
 PUBLISHER: American Society for Microbiology
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Due to concerns about the current therapeutic modalities for Helicobacter pylori infection, e.g., the increased emergence of drug-resistant strains and the adverse reactions of drugs currently administered, there is a need to develop an anti-H. pylori agent with higher efficacy and less toxicity. The antibacterial activity of TG44, an anti-H. pylori agent with a novel structural formula, against 54 clin. isolates of H. pylori was examined and compared with those of amoxicillin (AMX), clarithromycin (CLR), and metronidazole (MNZ). Consequently, TG44 inhibited the growth of H. pylori in an MIC range of 0.0625 to 1 µg/mL. The MIC ranges of AMX, CLR, and MNZ were 0.0078 to 8 µg/mL, 0.0156 to 64 µg/mL, and 2 to 128 µg/mL, resp. The antibacterial activity of TG44 against AMX-, CLR-, and MNZ-resistant strains was nearly comparable to that against drug-susceptible ones. In a pH range of 3 to 7, TG44 at 3.13 to 12.5 µg/mL exhibited potent bactericidal activity against H. pylori in the stationary phase of growth as early as 1 h after treatment began, in contrast to AMX, which showed no bactericidal activity at concns. of up to 50 µg/mL at the same time point of treatment. TG44 at 25 µg/mL exhibited no antibacterial activity against 13 strains of aerobic bacteria, suggesting that its antibacterial activity against H. pylori is potent and highly specific. The present study indicated that TG44 possesses antibacterial activity which manifests quickly and is potentially useful for eradicating not only the antibiotic-susceptible but also the antibiotic-resistant strains of H. pylori by monotherapy.

CC 10-5 (Microbial, Algal, and Fungal Biochemistry)

IT INDEXING IN PROGRESS

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

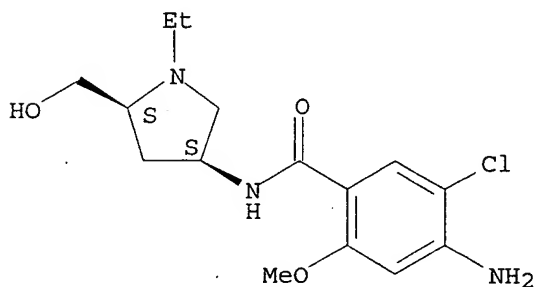
L80 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2000:172222 CAPLUS
 DOCUMENT NUMBER: 132:301171
 TITLE: Preparation and characterization of two crystalline forms of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide (TKS159)
 AUTHOR(S): Yanagi, Toshiharu; Mizoguchi, Jun-ichi; Adachi, Tsutomu; Sato, Seiji; Kodama, Kazuya; Anzai, Kinsei; Takagishi, Yasushi; Kamei, Chiaki; Fujiwara, Manabu; Matsushita, Takayuki; Yamashoji, Yuko; Inoue, Yoshihisa
 CORPORATE SOURCE: Research and Development Department, Teikoku Chemical Industries Co., Ltd., Hyogo, 664-0898, Japan
 SOURCE: Chemical & Pharmaceutical Bulletin (2000), 48(3), 366-369

PUBLISHER: CODEN: CPBTAL; ISSN: 0009-2363
 DOCUMENT TYPE: Pharmaceutical Society of Japan
 LANGUAGE: Journal
 English

- AB For 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide (TKS159), two polymorphs, forms α and β , were prepared and characterized by x-ray powder diffractometry, thermal anal., IR spectroscopy and ^{13}C -NMR spectroscopy, both in the solution and solid phases. The x-ray powder diffraction anal. gave different patterns for forms α and β . In the TG and DTA profiles, form β exhibited characteristic endo- and exothermic peaks at 112.7° and 116.2°, resp., due to the partial melting-induced phase transition to form α without accompanying weight loss, and these were followed by an addnl. endothermic peak at 138.2° due to fusion. For form α , only an endothermic peak at 137.8° due to fusion was observed. The IR spectroscopic analyses of forms α and β gave different absorption bands assigned to N-H and O-H stretching, N-H bending, and C=O stretching vibrations. From the data obtained by thermal anal., form α is thermodynamically more stable than form β .
- CC 75-7 (Crystallography and Liquid Crystals)
 Section cross-reference(s): 27
- IT 142228-17-9P, TKS159
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
 (preparation and characterization of crystalline forms of)
- IT 142228-17-9P, TKS159
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
 (preparation and characterization of crystalline forms of)
- RN 142228-17-9 CAPLUS
- CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6
 ACCESSION NUMBER: 1999:765890 CAPLUS
 DOCUMENT NUMBER: 132:122464
 TITLE: Synthesis and pharmacological activity of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide (TKS159) and its optical isomers
 AUTHOR(S): Yanagi, Toshiharu; Katajima, Akihiko; Anzai, Kinsei; Kodama, Kazuya; Mizoguchi, Jun-Ichi; Fujiwara, Hiromichi; Sakiyama, Hideyo; Kamoda, Osamu;

CORPORATE SOURCE: Kamei, Chiaki
Research and Development Department, Teikoku Chemical
Industries Co., Ltd., Hyogo, 664-0898, Japan

SOURCE: Chemical & Pharmaceutical Bulletin (1999), 47(11),
1650-1654
CODEN: CPBTAL; ISSN: 0009-2363

PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

AB TKS159 and its optical isomers were prepared from optically active
4-amino-1-ethyl-2-hydroxymethylpyrrolidine di-p-toluenesulfonates, which
were prepared from a com. available trans-4-hydroxy-L-proline. The absolute
configurations of TKS159 and its isomers were spectroscopically determined. All
the isomers showed a relatively potent affinity for 5-hydroxytryptamine 4
(5-HT₄) receptors in a radioligand binding assay
([³H]GR113808). The other isomers were less effective than TKS159 for the
gastric emptying of a phenol red semisolid meal in rats. All this
suggests that the most potent of the isomers was 4-amino-5-chloro-2-
methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide
(TKS159).

CC 27-10 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST hydroxymethylpyrrolidinylbenzamide TKS159 isomer prepn
serotonergic; gastric emptying
hydroxymethylpyrrolidinylbenzamide TKS159 isomer

IT 5-HT agonists
(5-HT₄; preparation and pharmacol. activity of TKS159
and its optical isomers)

IT Gastric emptying
(preparation and pharmacol. activity of TKS159 and its optical isomers)

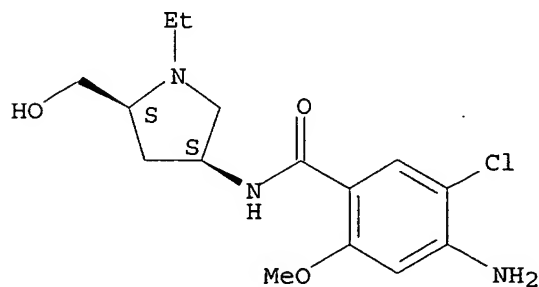
IT 142228-17-9P, TKS159 142228-19-1P 142228-20-4P
142228-21-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological
study); PREP (Preparation)
(preparation and pharmacol. activity of TKS159 and its optical isomers)

IT 142228-17-9P, TKS159 142228-19-1P 142228-20-4P
142228-21-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological
study); PREP (Preparation)
(preparation and pharmacol. activity of TKS159 and its optical isomers)

RN 142228-17-9 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-
pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

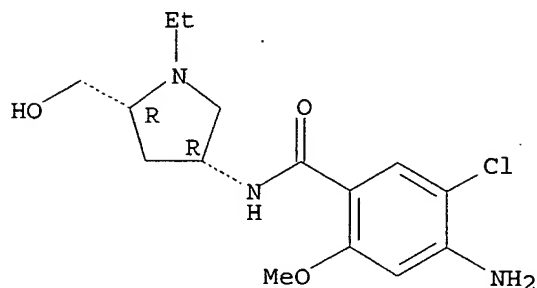
Absolute stereochemistry.



10/27/2006

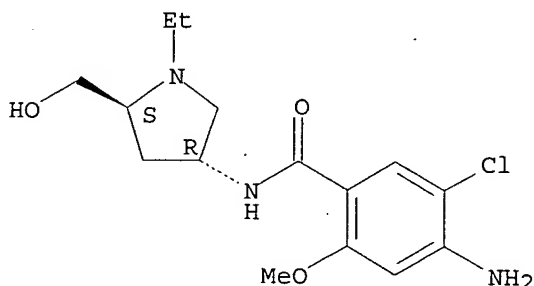
RN 142228-19-1 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[(3R,5R)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



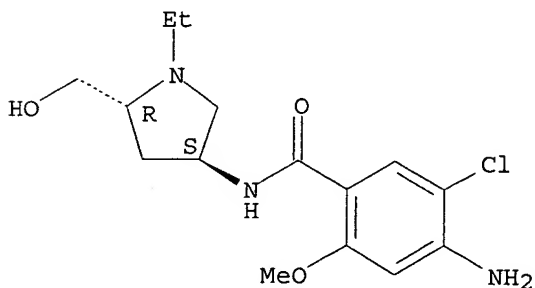
RN 142228-20-4 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[(3R,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 142228-21-5 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[(3S,5R)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:252358 CAPLUS
DOCUMENT NUMBER: 140:264507

Searched by John DiNatale x2-2557

Page 16

TITLE: Medicinal composition for improving *digestive tract* movement
 INVENTOR(S): Kitajima, Akihiko; Kamoda, Osamu; Ohsako, Akihiro; Yanagi, Toshiharu
 PATENT ASSIGNEE(S): Nagase Chemtex Corporation, Japan
 SOURCE: PCT Int. Appl., 37 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004024143	A1	20040325	WO 2002-JP9390	20020912
W: AE, AG, AL, AM, AU, AZ, BA, BB, BR, BY, BZ, CA, CN, CO, CR, CU, DM, DZ, EC, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, RU, SG, SI, TJ, TM, TN, TT, UA, US, UZ, VC, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002335161	A1	20040430	AU 2002-335161	20020912
EP 1547593	A1	20050629	EP 2002-807809	20020912
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CN 1668295	A	20050914	CN 2002-829602	20020912
US 2005239861	A1	20051027	US 2005-526780	20050520
			WO 2002-JP9390	A 20020912

PRIORITY APPLN. INFO.:

AB An ameliorant for improving the movement of the *digestive tract* which is rich in binding affinity for a *serotonin* receptor 4 (5HT₄), causes no disorders such as arteritis and thrombus formation, and contains as an active ingredient 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof, which is a product of metabolism of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof; a medicinal composition for improving the movement of the *digestive tract* which comprises the ameliorant and a pharmaceutically acceptable support, is rich in binding affinity for a *serotonin* receptor 4 (5HT₄), and causes no disorders such as arteritis and thrombus formation; and a treatment for enhancing the movement of the *digestive tract* which comprises using the medicinal composition

IC ICM A61K031-40
 ICS A61P001-14; C07D207-08

CC 1-9 (Pharmacology),
 Section cross-reference(s): 63

ST *hypoperistalsis digestive tract* movement
serotonin receptor arteritis thrombus

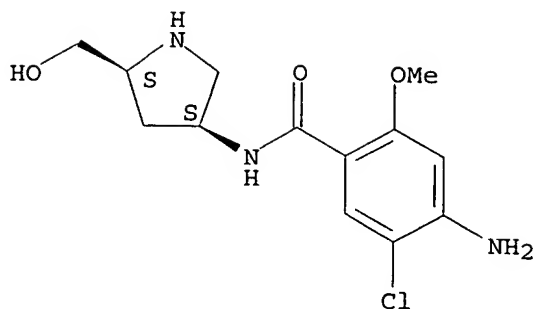
IT 5-HT agonists
 (5-HT₄; medicinal composition for improving *digestive tract* movement)

IT Dopamine receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (D2; medicinal composition for improving *digestive tract* movement)

IT Artery, disease
 Inflammation
 (arteritis; medicinal composition for improving *digestive tract* movement)

- tract movement)
- IT **Digestive tract, disease**
(*hypoperistalsis*; medicinal composition for improving **digestive tract** movement)
- IT **Thrombus**
(medicinal composition for improving **digestive tract** movement)
- IT **Drug delivery systems**
(tablets; medicinal composition for improving **digestive tract** movement)
- IT **5-HT receptors**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type **5-HT4**; medicinal composition for improving **digestive tract** movement)
- IT **672285-79-9P**
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(medicinal composition for improving **digestive tract** movement)
- IT 24201-13-6, 4-Acetylamino-5-chloro-2-methoxy-benzoic acid 33996-30-4,
4-Hydroxy-L-proline-ethyl ester hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(medicinal composition for improving **digestive tract** movement)
- IT 33996-28-0P 672285-80-2P 672285-81-3P 672285-82-4P 672285-83-5P
672285-84-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(medicinal composition for improving **digestive tract** movement)
- IT **672285-79-9P**
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(medicinal composition for improving **digestive tract** movement)
- RN 672285-79-9 CAPLUS
- CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)

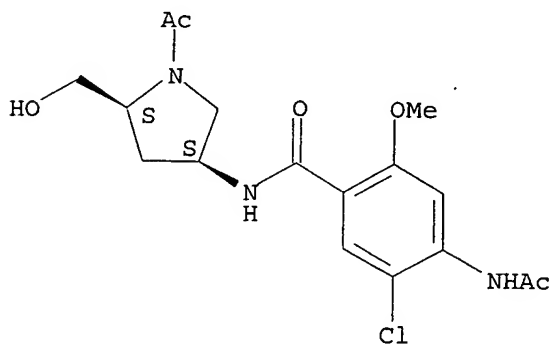
Absolute stereochemistry.



● HCl

IT 672285-84-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (medicinal composition for improving *digestive tract*
 movement)
 RN 672285-84-6 CAPLUS
 CN Benzamide, 4-(acetylamino)-N-[(3S,5S)-1-acetyl-5-(hydroxymethyl)-3-
 pyrrolidinyl]-5-chloro-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1997:503261 CAPLUS
 DOCUMENT NUMBER: 127:113344
 TITLE: Trans-4-guanidinomethylcyclohexanecarboxylic acid
 esters for inhibition of Helicobacter pylori
 INVENTOR(S): Kamoda, Osamu; Yanagi, Toshiharu;
 Tamaki, Eiji; Sato, Seiji; Mizoguchi, Jun-ichi
 PATENT ASSIGNEE(S): Teikoku Chemical Industries Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 26 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9723207	A1	19970703	WO 1996-JP3723	19961220
W: AU, CN, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9711716	A1	19970717	AU 1997-11716	19961220
EP 870500	A1	19981014	EP 1996-942589	19961220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 3468244	B2	20031117	JP 1997-523501	19961220
TW 457086	B	20011001	TW 1996-85115861	19970120
TW 225786	B1	20050101	TW 2001-90111426	19970120
US 6444703	B1	20020903	US 1998-91588	19980812
US 2002123508	A1	20020905		
AU 763893	B2	20030731	AU 2001-19709	20010212
PRIORITY APPLN. INFO.:				
			JP 1995-354660	A 19951222
			WO 1996-JP3723	W 19961220

AB A drug composition which comprises a combination of 4-[4-(4-methylbenzyloxycarbonyl)phenyl]phenyl trans-4-guanidinomethylcyclohexanecarboxylate (I) or an acid addition salt thereof and a cyclodextrin, especially β -cyclodextrin, is suitable for removing or exterminating *Helicobacter pylori*. I·HCl 4 g was dissolved in 120 mL aqueous solution containing 8.46 g β -cyclodextrin and freeze-dried. The product showed an improved solubility

IC ICM A61K031-24
ICS A61K047-40

CC 63-5 (Pharmaceuticals)

L80 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:431362 CAPLUS

DOCUMENT NUMBER: 125:86328

TITLE: Preparation of guanidinomethylcyclohexanecarboxylic acid aryl ester derivatives as antibacterial agents against *Helicobacter pylori* infection

INVENTOR(S): Kamoda, Osamu; Fujiwara, Hiromichi;
Yanagi, Toshiharu

PATENT ASSIGNEE(S): Teikoku Chemical Industries Co., Ltd., Japan

SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9606825	A1	19960307	WO 1995-JP1725	19950830
W: JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 775692	A1	19970528	EP 1995-930012	19950830
EP 775692	B1	20001206		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
EP 989112	A2	20000329	EP 1999-124756	19950830
EP 989112	A3	20001115		
EP 989112	B1	20040414		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
AT 197950	E	20001215	AT 1995-930012	19950830
ES 2153902	T3	20010316	ES 1995-930012	19950830
PT 775692	T	20010531	PT 1995-930012	19950830

crystals, concentrated in vacuo, treated with dry pyridine, ice-cooled, treated with 1.50 g trans-4-guanidinomethylcyclohexanecarboxylic acid hydrochloride, and stirred overnight under water-cooling to give 2.44 g trans-I.HCl (Ar = Q). The latter compound showed min. inhibitory concentration of 0.20, 0.39, and >25 µg/mL against *Helicobacter pylori* ATCC 43504 and ATCC 43629 and *Escherichia coli* NIH JC-2, resp. Each dispersant, capsule, and suspension formulation containing I (Ar = Q1) was prepared

IC ICM C07C279-14
ICS A61K031-215; A61K031-275

CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1

L80 ANSWER 7 OF 12 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 3

ACCESSION NUMBER: 2002:545501 BIOSIS
DOCUMENT NUMBER: PREV200200545501
TITLE: Cyclohexane carbocyclic ester derivative and cyclodextrin complex and composition for treatment of helicobacter pylori infections.

AUTHOR(S): Kamoda, Osamu [Inventor, Reprint author];
Yanagi, Toshiharu [Inventor]; Tamaki, Eiji
[Inventor]; Sato, Seiji [Inventor]; Mizoguchi, Jun-ichi
[Inventor]

CORPORATE SOURCE: Hyogo, Japan
ASSIGNEE: Teikoku Chemical Industries Co., Ltd., Osaka,
Japan

PATENT INFORMATION: US 6444703 20020903
SOURCE: Official Gazette of the United States Patent and Trademark
Office Patents, (Sep. 3, 2002) Vol. 1262, No. 1.
<http://www.uspto.gov/web/menu/patdata.html>. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Oct 2002
Last Updated on STN: 23 Oct 2002

ABSTRACT: The present invention relates to a pharmaceutical composition which is appropriate for eradication or extermination of *Helicobacter pylori* wherein [4-[4-(4-methylbenzyloxycarbonyl)phenyl]phenyl trans-4-guanidinomethylcyclohexanecarboxylate or an acid addition salt thereof are compounded and it also relates to a complex consisting them.

NAT. PATENT. CLASSIF.: 514553000

CONCEPT CODE: Pharmacology - General 22002
Physiology and biochemistry of bacteria 31000
Chemotherapy - General, methods and metabolism 38502
Chemotherapy - Antibacterial agents 38504

INDEX TERMS: Major Concepts
Pharmacology

INDEX TERMS: Diseases
Helicobacter pylori infection: bacterial disease
Helicobacter Infections (MeSH)

INDEX TERMS: Chemicals & Biochemicals
[4-[4-(4-methylbenzyloxycarbonyl)phenyl]phenyl trans-4-guanidinomethylcyclohexanecarboxylate:
antibacterial-drug, antiinfective-drug; cyclodextrin
complex: antibacterial-drug, antiinfective-drug;
cyclohexane carbocyclic ester derivative:

antibacterial-drug, antiinfective-drug

ORGANISM: Classifier
Aerobic Helical or Vibrioid Gram-Negatives 06210
Super Taxa
Eubacteria; Bacteria; Microorganisms
Organism Name
Helicobacter pylori: pathogen
Taxa Notes
Bacteria, Eubacteria, Microorganisms

L80 ANSWER 8 OF 12 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 4

ACCESSION NUMBER: 2001:521744 BIOSIS
DOCUMENT NUMBER: PREV200100521744
TITLE: Guanidinomethyl cyclohexane carboxylic acid ester
derivatives.

AUTHOR(S): Kamoda, Osamu [Inventor, Reprint author];
Fujiwara, Hiromichi [Inventor]; Yanagi, Toshiharu
[Inventor]

CORPORATE SOURCE: Itami, Japan
ASSIGNEE: Teikoku Chemical Industries Co., Ltd., Osaka,
Japan

PATENT INFORMATION: US 6284791 20010904
SOURCE: Official Gazette of the United States Patent and Trademark
Office Patents, (Sep. 4, 2001) Vol. 1250, No. 1. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Nov 2001
Last Updated on STN: 23 Feb 2002

ABSTRACT: A compound represented by general formula (I-2) or a pharmaceutically
acceptable acid-addition salt thereof, useful as an anti-microbial against
Helicobacter pylori and as a medicinal composition for treating Helicobacter
pylori infection, wherein Ar represents phenyl, biphenyl or naphthyl each
having at least one substituent selected from the group consisting of
halogen, cyano, nitro, carboxy, C1 -C18 alkyl, C1 -C18 alkoxy, C3 -C18
cycloalkyl, C7 -C18 aralkyl, C8 -C18 arylalkenyl, C7 -C18 aralkyloxy,
optionally substituted phenoxy, optionally substituted C2 -C19 alkoxy carbonyl,
and optionally substituted C8 -C19 aralkyloxy carbonyl, provided the case where
Ar represents phenyl substituted by halogen, cyano, nitro, carboxy, C1 -C18
alkyl, optionally substituted C2 -C19 alkoxy carbonyl or C8 -C19
aralkyloxy carbonyl is expected.

NAT. PATENT. CLASSIF.: 514529000

CONCEPT CODE: General biology - Miscellaneous 00532

INDEX TERMS: Major Concepts
Methods and Techniques; Pharmacology

INDEX TERMS: Diseases
Helicobacter pylori infection: bacterial disease,
treatment
Helicobacter Infections (MeSH)

INDEX TERMS: Chemicals & Biochemicals
guanidinomethyl cyclohexane carboxylic acid ester
derivatives: antibacterial-drug

ORGANISM: Classifier
Aerobic Helical or Vibrioid Gram-Negatives 06210
Super Taxa
Eubacteria; Bacteria; Microorganisms
Organism Name
Helicobacter pylori
Taxa Notes

APPLICATION INFO.: US 2003-623135 A1 20030718 (10)
 RELATED APPLN. INFO.: Division of Ser. No. US 2000-721182, filed on 22 Nov
 2000, GRANTED, Pat. No. US 6831190 Division of Ser. No.
 US 1997-793728, filed on 28 Feb 1997, GRANTED, Pat. No.
 US 6284791

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1994-243489	19940830
	JP 1994-243490	19940830
	JP 1994-248270	19940905
	JP 1994-252655	19940909
	WO 1995-JP1725	19950830
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	EDWARDS & ANGELL, LLP, P.O. BOX 55874, BOSTON, MA, 02205	
NUMBER OF CLAIMS:	8	
EXEMPLARY CLAIM:	CLM-01-14	
LINE COUNT:	2064	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		
AB	The invention relates to novel and valuable intermediate compounds of the general formula (VIII) which can be used for the preparation of novel compounds comprising an antibacterial action, especially with a strong antibacterial action against helicobacter pylori, and pharmaceutically acceptable salts thereof. In the general formula (VIII) X is hydrogen or halogen, Y is hydrogen or a substituted or unsubstituted aralkyloxycarbonyl group having 8-19 carbon atoms, Z is hydrogen, a substituted aralkyloxycarbonyl group having 8-19 carbon atoms or a substituted alkoxycarbonyl group having 2-19 carbon atoms, except that X, Y and Z are all hydrogen. ##STR1##	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IN *Kamoda, Osamu*, Itami-shi, JAPAN
 IN *Yanagi, Toshiharu*, Itami-shi, JAPAN

L80 ANSWER 11 OF 12 USPATFULL on STN

ACCESSION NUMBER: 2005:275296 USPATFULL
 TITLE: Medicinal composition
 INVENTOR(S): *Kitajima, Akihiko*, Fukuchiyama-shi, JAPAN
Kamoda, Osamu, Fukuchiyama-shi, JAPAN
Ohsako, Akihiro, Fukuchiyama-shi, JAPAN
Yanagi, Toshiharu, Osaka-shi, JAPAN

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005239861	A1	20051027
APPLICATION INFO.:	US 2003-526780	A1	20020912 (10)
	WO 2002-JP9390		20020912
			20050520 PCT 371 date
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	WENDEROTH, LIND & PONACK, L.L.P., 2033 K STREET N. W., SUITE 800, WASHINGTON, DC, 20006-1021, US		
NUMBER OF CLAIMS:	10		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	3 Drawing Page(s)		
LINE COUNT:	859		
CAS INDEXING IS AVAILABLE FOR THIS PATENT.			
AB	The present invention relates to an ameliorant for improving the		

movement of the *digestive tract* comprising, as an active ingredient, 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof which is a metabolite of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof, having high binding affinity for a *serotonin* receptor 4 (*5HT*.sub.4) and causing no arteritis and thrombus formation; a medicinal composition for improving the movement of the *digestive tract* comprising the said ameliorant and a pharmaceutically acceptable carrier; and a treating method for promoting the movement of the *digestive tract*, which comprises using the said medicinal composition for improving the movement of the *digestive tract*.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IN *Kitajima, Akihiko*, Fukuchiyama-shi, JAPAN

IN *Kamoda, Osamu*, Fukuchiyama-shi, JAPAN

IN *Ohsako, Akihiro*, Fukuchiyama-shi, JAPAN

IN *Yanagi, Toshiharu*, Osaka-shi, JAPAN

AB The present invention relates to an ameliorant for improving the movement of the *digestive tract* comprising, as an active ingredient, 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof which is a metabolite of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof, having high binding affinity for a *serotonin* receptor 4 (*5HT*.sub.4) and causing no arteritis and thrombus formation; a medicinal composition for improving the movement of the *digestive tract* comprising the said ameliorant and a pharmaceutically acceptable carrier; and a treating method for promoting the movement of the *digestive tract*, which comprises using the said medicinal composition for improving the movement of the *digestive tract*.

SUMM The present invention relates to an ameliorant for improving the movement of the *digestive tract* of a human and an animal containing as an active ingredient a compound which is suitable for activating the movement of the *digestive tract*, inter alia, *stomach* to rapidly eliminate abnormal retention of an ingested food in the organ, has a peripheral acting site, and has no . . . comprising the active ingredient and a pharmaceutically acceptable carrier, a method for improving disorder of the movement dysfunction of the *digestive tract* comprising administering a composition containing an effective amount of the active compound to a patient, and use of the compound.

SUMM . . . compound having a generic name of metoclopramide is widely known as a compound having nature of promoting the movement of *stomach*, but induces extrapyramidal disorder and other undesirable disorders due to action on central nervous system. In addition, a compound having a generic name of cisapride has been put into practice as a *digestive tract* movement activator, but use thereof has been stopped due to inducement of ventricular arrhythmia.

SUMM . . . extremely weak action on central nervous system is known as a compound having action of promoting the movement of the *digestive tract*, inter alia, *stomach* (JP-A-17434/1993). However, the present applicant progressed development of TKS159 which is a representative compound of the invention of the above. . . that 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof is a compound having the ability of improving the movement of the *digestive*

tract equivalent to or superior over that of TKS159 or an acid addition salt thereof. That is, it was found out. . . thrombus formation, arteritis, encephalomalacia and the like can be effectively used as an ameliorant for improving the movement of the **digestive tract** containing this compound as an active ingredient. Needless to say, it is natural that desired attribute of a drug used.

SUMM . . . invention has been made based on the aforementioned findings, and relates to an ameliorant for improving the movement of the **digestive tract**, which avoids side effect such as arteritis, containing 4-amino-5-chloro-2-methoxy-N-[(2S, 4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof as an active ingredient..

SUMM The ameliorant for improving the movement of the **digestive tract** of the present invention and a novel medicinal composition containing the same relate to a novel medicinal composition comprising a.

SUMM . . . salt is superior over TKS159 or an acid addition salt thereof in the ability to improve the movement of the **digestive tract**. Further, it was also made clear that 4-amino-5-chloro-2-methoxy-N-[(2S, 4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof acts as an agonist such that binding with a **serotonin** 4 (5HT.sub.4) receptor is preferential to binding to other receptor, for example, a dopamine D.sub.2 receptor.

SUMM . . . various new findings and, according to the present invention, there are provided an ameliorant for improving the movement of the **digestive tract** containing as an active ingredient 4-amino-5-chloro-2-methoxy-N-[(2S, 4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof, which has high binding affinity for a **serotonin** receptor 4 (5HT.sub.4), and can avoid occurrence of side effect such as thrombus formation, arteritis and the like inevitably caused concomitantly in administration.

SUMM . . . serious side effect is confirmed. That is, the present invention relates to an ameliorant for improving the movement of the **digestive tract** which has been confirmed to be an effective and safe medicine not accompanied with occurrence of side effect.

SUMM (1) an ameliorant for improving the movement of the **digestive tract** comprising as an active ingredient 4-amino-5-chloro-2-methoxy-N-[(2S, 4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof, which has high binding affinity for a **serotonin** receptor 4 (5HT.sub.4), and does not cause arteritis and thrombus formation,

SUMM (2) a medicinal composition for improving the movement of the **digestive tract**, comprising as an active ingredient 4-amino-5-chloro-2-methoxy-N-[(2S, 4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof, which has high binding affinity for a **serotonin** receptor 4 (5HT.sub.4), and does not cause arteritis and thrombus formation, and a pharmaceutically acceptable carrier,

SUMM (3) a treating method for promoting the movement of the **digestive tract**, which comprises using an ameliorant for improving the movement of the **digestive tract** comprising as an active ingredient 4-amino-5-chloro-2-methoxy-N-[(2S, 4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof, which has high binding affinity for a **serotonin** receptor 4 (5HT.sub.4), and does not cause arteritis and thrombus formation, or using a medicinal composition for improving the movement of the **digestive tract** comprising the

ameliorant and a pharmaceutically acceptable carrier,

SUMM (4) a method for improving the movement of the **digestive tract** of a human or an animal, while avoiding occurrence of arteritis, thrombus formation or encephalomalacia, which comprises administering 4-amino-5-chloro-2-methoxy-N-[(2S, 4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide.

DRWD FIG. 1 shows a change in binding affinity for a **serotonin** receptor 4, of a specimen drug. An abscissa axis indicates a concentration (molar concentration; logarithmic expression) of a specimen drug, and an ordinate axis indicates a ratio of binding of a **serotonin** receptor 4 and [.sup.3H] GR113808. .largecircle. - - - .largecircle. indicates a specimen compound obtained in Example 9, and .circle-solid. . . .circle-solid. indicates TKS159 hydrochloride. As a concentration of a specimen drug grows higher, an amount of [.sup.3H]GR113808 bound to a **serotonin** receptor 4 is reduced. That is, it is indicated that a specimen drug binds to a **serotonin** receptor 4, antagonizing [.sup.3H]GR113808 binding to the **serotonin** receptor 4. It is seen that affinity of a specimen drug obtained in Example 9 for a **serotonin** receptor 4 is stronger as compared with affinity of TKS159 hydrochloride.

DETD . . . compound of the formula (III) can be used like TM161, since it exerts effect of improving the movement of the **digestive tract** more excellent than that of TKS159 while avoiding side effect such as thrombus formation, arteritis and encephalomalacia. Examples of a . . .

DETD 4-Amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide of the present invention or an acid addition salt thereof, which has high binding affinity for a **serotonin** receptor 4 (5HT.sub.4) and does not cause arteritis, thrombus formation and the like is a metabolite of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt. . . .

DETD Thus, an ameliorant for improving the movement of the **digestive tract** which has high binding affinity for a **serotonin** receptor 4 (5HT.sub.4) and can avoid side effect occurred concomitantly in TKS159 or an acid addition salt thereof such as arteritis and thrombus. . . .

DETD 4-Amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof obtained herein, which is an ameliorant for improving the movement of the **digestive tract** having high binding affinity for a **serotonin** receptor 4 (5HT.sub.4) and being capable of avoiding side effect that concomitantly occurs in association with TKS159 or an acid addition salt thereof, . . . a pharmaceutically acceptable suitable carrier, and is put into practice as a medicinal composition for improving the movement of the **digestive tract**.

DETD As the preparation of a formulated medicinal composition of the present invention for improving the movement of the **digestive tract** comprising 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof which is an ameliorant for improving the movement of the **digestive tract**, having high binding affinity for a **serotonin** receptor 4 (5HT.sub.4) and being capable of avoiding side effect that concomitantly occurs in association with TKS159 or an acid addition salt thereof. . . the aforementioned carriers. For example, when a preparation which is a formulated medicinal composition for improving the movement of the **digestive tract** is a tablet, a prescribed amount of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-

pyrrolidinyl]benzamide or an acid addition salt thereof, which is an ameliorant for improving the movement of the **digestive tract**, having high binding affinity for a **serotonin** receptor 4 (**5HT.sub.4**) and being capable of avoiding side effect that concomitantly occurs in association with TKS159 or an acid addition salt thereof.

DETD . . . content of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof which is an ameliorant for improving the movement of the **digestive tract** having high binding affinity for a **serotonin** receptor 4 (**5HT.sub.4**) and being capable of avoiding side effect that concomitantly occurs in association with TKS159 or an acid addition salt thereof.

DETD 4-Amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof which is an ameliorant for improving the movement of the **digestive tract** having high binding affinity for a **serotonin** receptor 4 (**5HT.sub.4**) and being capable of avoiding side effect that concomitantly occurs in association with TKS159 or an acid addition salt thereof, . . . toxicity test, and is therefore suitable in oral administration. There are provided an ameliorant for improving the movement of the **digestive tract** comprising, as an active ingredient, 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof which is a metabolite of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof, having high binding affinity for a **serotonin** receptor 4 (**5HT.sub.4**) and causing no arteritis and thrombus formation, and a medicinal composition for improving the movement of the **digestive tract** comprising the same and a carrier.

DETD Measurement of Action of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide monohydrochloride on **serotonin** receptor 4

DETD . . . pig was homogenized in a 50 mM HEPES-NaOH buffer (pH 7.4), and centrifugation and suspension were repeated to prepare a **serotonin** receptor 4 sample. The receptor sample was reacted with a solution containing a 0.1 nM radioactive ligand of [³H]-GR113808 and. . . of the filter was measured using a scintillation counter (LS6500 Beckman), so that affinity of the specimen drug for a **serotonin** receptor 4 was measured. Separately, the same procedure was also performed regarding TKS159 hydrochloride, and the affinity was compared.

DETD . . . specimen was forcibly administered orally at 9 o'clock to 12 o'clock for 28 days once a day using a rat **stomach** tube. Only a 0.5% aqueous methylcellulose solution was administered at 10 ml/kg to a control group.

DETD Regarding the drug obtained in Example 9, a degree of action of promoting the movement of the **digestive tract** was measured using an esophagus sample extracted from a rat.

DETD . . . one case, necrosis of an artery septum and surrounding cell infiltration were recognized in cerebellum, lung, coronary artery, liver, bladder, **stomach**, vagina, **intestine** and diaphragm. Separately, beagle dogs (female and male) were divided into 4 groups containing 5, 3, 3 and 5 dogs.

DETD In the present invention, an ameliorant for improving the movement of the **digestive tract** comprising, as an active ingredient, 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof which has high binding affinity for a **serotonin** receptor 4 (**5HT.sub.4**) and capable of avoiding side effect occurrence such as thrombus

formation and arteritis concomitantly caused inevitably in administration of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide. . .

CLM

What is claimed is:

1. An ameliorant for improving the movement of the *digestive tract*, comprising as an active ingredient 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof which has high binding affinity for a *serotonin* receptor 4 (*5HT*.sub.4) and does not cause arteritis and thrombus formation.
2. A medicinal composition for improving the movement of the *digestive tract*, comprising as an active ingredient 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof which has high binding affinity for a *serotonin* receptor 4 (*5HT*.sub.4) and does not cause arteritis and thrombus formation, and a pharmaceutically acceptable carrier.
3. A treating method for promoting the movement of the *digestive tract*, which comprises using an ameliorant for improving the movement of the *digestive tract* comprising as an active ingredient 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof which has high binding affinity for a *serotonin* receptor 4 (*5HT*.sub.4) and does not cause arteritis and thrombus formation, or using a medicinal composition for improving the movement of the *digestive tract* comprising the ameliorant and a pharmaceutically acceptable carrier.
4. A method for improving the movement of the *digestive tract* of a human or an animal while avoiding occurrence of arteritis, thrombus formation or encephalomalacia, which comprises administering 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or. . .

IT 672285-79-9P

(medicinal composition for improving digestive tract movement)

IT 33996-28-0P 672285-80-2P 672285-81-3P 672285-82-4P 672285-83-5P
672285-84-6P

(medicinal composition for improving digestive tract movement)

IT 672285-79-9P

(medicinal composition for improving digestive tract movement)

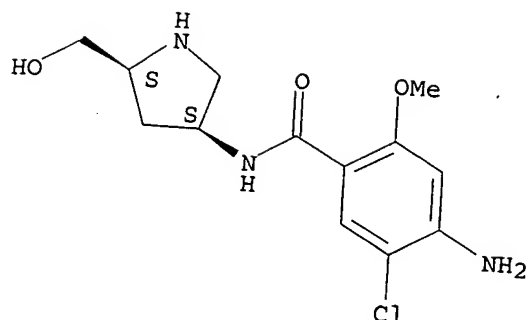
RN 672285-79-9 USPTAFULL

CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

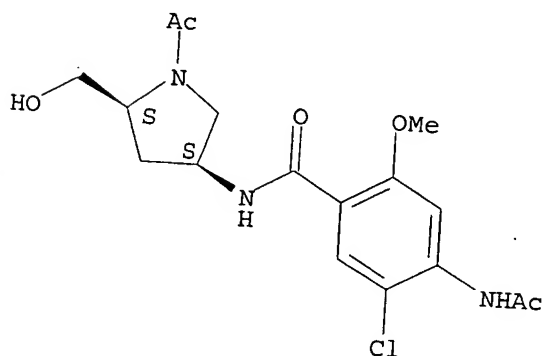
10/27/2006

10/27/2006



● HCl

IT 672285-84-6P
 (medicinal composition for improving digestive tract movement)
 RN 672285-84-6 USPATFULL
 CN Benzamide, 4-(acetylamino)-N-[(3S,5S)-1-acetyl-5-(hydroxymethyl)-3-pyrrolidinyl]-5-chloro-2-methoxy- (9CI) (CA INDEX NAME)
 Absolute stereochemistry.



L80 ANSWER 12 OF 12 USPATFULL on STN
 ACCESSION NUMBER: 2004:317320 USPATFULL
 TITLE: Guanidinomethyl cyclohexane carboxylic acid ester derivatives
 INVENTOR(S): Kamoda, Osamu, Itami, JAPAN
 Fujiwara, Hiromichi, Itami, JAPAN
 PATENT ASSIGNEE(S): Yanagi, Toshiharu, Itami, JAPAN
 Teikoku Chemical Industries Co., Ltd., Osaka, JAPAN
 (non-U.S. corporation)

PATENT INFORMATION:
 APPLICATION INFO.:
 RELATED APPLN. INFO.:

NUMBER	KIND	DATE
US 6831190	B1	20041214
US 2000-721182		20001122 (9)
Division of Ser. No. US 1997-793728, filed on 28 Feb 1997		

NUMBER	DATE

Searched by John DiNatale x2-2557

PRIORITY INFORMATION: JP 1994-243489 19940830
JP 1994-243490 19940830
JP 1994-248270 19940905
JP 1994-252655 19940909

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Barts, Samuel
LEGAL REPRESENTATIVE: Corless, Peter F., Alexander, John B., Edwards & Angell, LLP
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 2000

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to novel and valuable intermediate compounds of the general formula (VIII) which can be used for the preparation of novel compounds comprising an antibacterial action, especially with a strong antibacterial action against helicobacter pylori, and pharmaceutically acceptable salts thereof. In the general formula (VIII) X is hydrogen or halogen, Y is hydrogen or a substituted or unsubstituted aralkyloxycarbonyl group having 8-19 carbon atoms, Z is hydrogen, a substituted aralkyloxycarbonyl group having 8-19 carbon atoms or a substituted alkoxycarbonyl group having 2-19 carbon atoms, except that X, Y and Z are all hydrogen. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IN Kamoda, Osamu, Itami, JAPAN
IN Yanagi, Toshiharu, Itami, JAPAN

=> file registry

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STRUCTURE/
TEXT
SEARCH

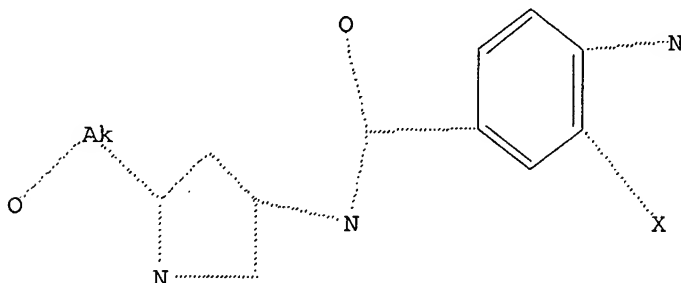
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

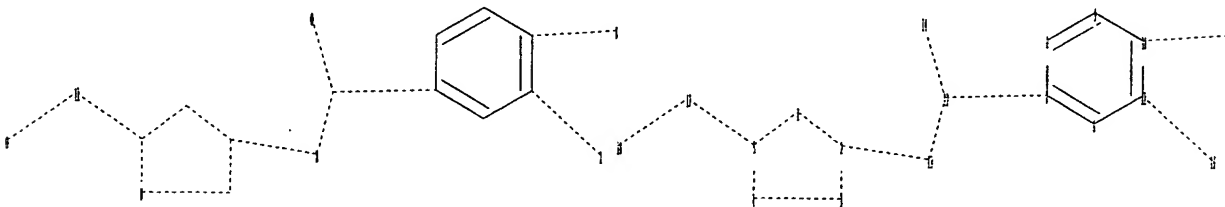
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L5

STR



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chain bonds :

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 1-2 1-5 2-3 2-13 3-4 4-5 5-17 7-12 10-15 11-16 12-13 12-14 17-18
 normalized bonds :
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Match level :

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100.0% PROCESSED 11082 ITERATIONS
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47 ANSWERS

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FILE COVERS 1907 - 26 Oct 2006 VOL 145 ISS 18
 FILE LAST UPDATED: 25 Oct 2006 (20061025/ED)

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 'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d que nos L8

L5 STR
 L7 47 SEA FILE=REGISTRY SSS FUL L5
 L8 18 SEA FILE=CAPLUS ABB=ON PLU=ON L7

=> d que nos L23

L5 STR

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L13         4188 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?PERISTAL?/BI
L14         249583 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?DIGEST?/BI
L15         288318 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?INTESTIN?/BI
L16         43191 SEA FILE=CAPLUS ABB=ON  PLU=ON  (5HT OR 5 HT?)/BI
L17         77545 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?SEROTONIN?/BI
L18         22550 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?ILEUM?/BI
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L20         31539 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?DUODEN?/BI
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L81 15 (L8 OR L23) NOT L75

=> file medline

FILE 'MEDLINE' ENTERED AT 13:51:10 ON 26 OCT 2006

FILE LAST UPDATED: 25 Oct 2006 (20061025/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>). See also:

<http://www.nlm.nih.gov/mesh/>
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> d que nos L46

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L16         43191 SEA FILE=CAPLUS ABB=ON PLU=ON (5HT OR 5 HT?)/BI
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L20         31539 SEA FILE=CAPLUS ABB=ON PLU=ON ?DUODEN?/BI
L21         139482 SEA FILE=CAPLUS ABB=ON PLU=ON TRACT#/BI
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=> s (L44 or L46 or L48) not L76

L82 3 (L44 OR L46 OR L48) NOT L76

=> file embase

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FILE COVERS 1974 TO 26 Oct 2006 (20061026/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default)
and biweekly.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> d que nos L53

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=> d que nos L54

L54 4 SEA FILE=EMBASE ABB=ON PLU=ON FAUC65 OR TKS159

=> d que nos L56

10/27/2006

```
L5          STR
L7          47 SEA FILE=REGISTRY SSS FUL L5
L11         105205 SEA FILE=CAPLUS ABB=ON PLU=ON ?STOMACH?/BI
L12         42051 SEA FILE=CAPLUS ABB=ON PLU=ON ?MOTIL?/BI
L13         4188 SEA FILE=CAPLUS ABB=ON PLU=ON ?PERISTAL?/BI
L14         249583 SEA FILE=CAPLUS ABB=ON PLU=ON ?DIGEST?/BI
L15         288318 SEA FILE=CAPLUS ABB=ON PLU=ON ?INTESTIN?/BI
L16         43191 SEA FILE=CAPLUS ABB=ON PLU=ON (5HT OR 5 HT?)/BI
L17         77545 SEA FILE=CAPLUS ABB=ON PLU=ON ?SEROTONIN?/BI
L18         22550 SEA FILE=CAPLUS ABB=ON PLU=ON ?ILEUM?/BI
L19         18576 SEA FILE=CAPLUS ABB=ON PLU=ON ?JEJUN?/BI
L20         31539 SEA FILE=CAPLUS ABB=ON PLU=ON ?DUODEN?/BI
L21         139482 SEA FILE=CAPLUS ABB=ON PLU=ON TRACT#/BI
L22         171670 SEA FILE=CAPLUS ABB=ON PLU=ON ?GASTR?/BI
L52         SEL PLU=ON L7 1- CHEM : 49 TERMS
L53         7 SEA FILE=EMBASE ABB=ON PLU=ON L52
L54         4 SEA FILE=EMBASE ABB=ON PLU=ON FAUC65 OR TKS159
L56         7 SEA FILE=EMBASE ABB=ON PLU=ON (L53 OR L54) AND (L11 OR L12
OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21
OR L22)
```

=> s (L53 or L54 or L56) not L77

L83 5 (L53 OR L54 OR L56) NOT L77

=> file biosis

FILE 'BIOSIS' ENTERED AT 13:51:18 ON 26 OCT 2006
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FILE COVERS 1969 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 18 October 2006 (20061018/ED)

=> d que nos L61

```
L5          STR
L7          47 SEA FILE=REGISTRY SSS FUL L5
L60         SEL PLU=ON L7 1- CHEM : 49 TERMS
L61         3 SEA FILE=BIOSIS ABB=ON PLU=ON L60
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=> d que nos L62

L62 5 SEA FILE=BIOSIS ABB=ON PLU=ON FAUC65 OR TKS159

=> s L61-L62 not L78

L84 3 (L61 OR L62) NOT L78

=> file uspatall

FILE 'USPATFULL' ENTERED AT 13:51:21 ON 26 OCT 2006
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FILE 'USPAT2' ENTERED AT 13:51:21 ON 26 OCT 2006
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=> d que nos L69

L5 STR
L7 47 SEA FILE=REGISTRY SSS FUL L5
L69 4 SEA L7

=> d que nos L71

L5 STR
L7 47 SEA FILE=REGISTRY SSS FUL L5
L11 105205 SEA FILE=CAPLUS ABB=ON PLU=ON ?STOMACH?/BI
L12 42051 SEA FILE=CAPLUS ABB=ON PLU=ON ?MOTIL?/BI
L13 4188 SEA FILE=CAPLUS ABB=ON PLU=ON ?PERISTAL?/BI
L14 249583 SEA FILE=CAPLUS ABB=ON PLU=ON ?DIGEST?/BI
L15 288318 SEA FILE=CAPLUS ABB=ON PLU=ON ?INTESTIN?/BI
L16 43191 SEA FILE=CAPLUS ABB=ON PLU=ON (5HT OR 5 HT?)/BI
L17 77545 SEA FILE=CAPLUS ABB=ON PLU=ON ?SEROTONIN?/BI
L18 22550 SEA FILE=CAPLUS ABB=ON PLU=ON ?ILEUM?/BI
L19 18576 SEA FILE=CAPLUS ABB=ON PLU=ON ?JEJUN?/BI
L20 31539 SEA FILE=CAPLUS ABB=ON PLU=ON ?DUODEN?/BI
L21 139482 SEA FILE=CAPLUS ABB=ON PLU=ON TRACT#/BI
L22 171670 SEA FILE=CAPLUS ABB=ON PLU=ON ?GASTR?/BI
L69 4 SEA L7
L70 308291 SEA (L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR
L19 OR L20 OR L21 OR L22)
L71 3 SEA L69 AND L70

=> s (L69 or L71) not L79

L85 3 (L69 OR L71) NOT L79

=> dup rem L81 L82 L83 L84 L85

FILE 'CAPLUS' ENTERED AT 13:53:56 ON 26 OCT 2006
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FILE 'BIOSIS' ENTERED AT 13:53:56 ON 26 OCT 2006
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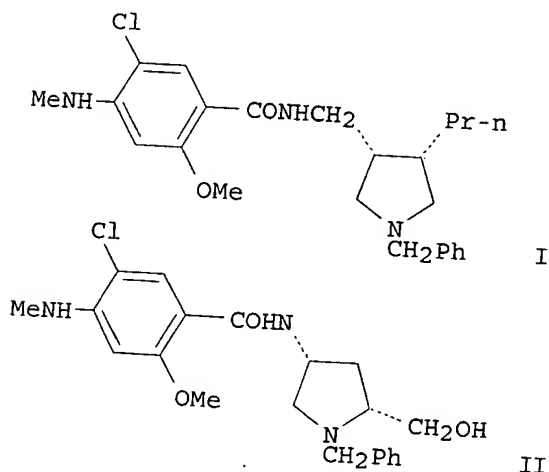
FILE 'USPATFULL' ENTERED AT 13:53:56 ON 26 OCT 2006
CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)
PROCESSING COMPLETED FOR L81
PROCESSING COMPLETED FOR L82
PROCESSING COMPLETED FOR L83
PROCESSING COMPLETED FOR L84
PROCESSING COMPLETED FOR L85

L86 22 DUP REM L81 L82 L83 L84 L85 (7 DUPLICATES REMOVED)
ANSWERS '1-15' FROM FILE CAPLUS
ANSWER '16' FROM FILE MEDLINE

ANSWERS '17-18' FROM FILE EMBASE
ANSWER '19' FROM FILE BIOSIS
ANSWERS '20-22' FROM FILE USPATFULL

=> d ibib abs hitind hitstr L86 1-15; d iall L86 16-19; d ibib abs kwic hitstr L86 20-22

L86 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2003:804055 CAPLUS
DOCUMENT NUMBER: 140:5276
TITLE: Ex-chiral pool synthesis and receptor binding studies of 4-substituted prolinol derivatives
AUTHOR(S): Heindl, Cornelia; Hubner, Harald; Gmeiner, Peter
CORPORATE SOURCE: Emil Fischer Center, Department of Medicinal Chemistry, Friedrich Alexander University, Erlangen, D-91052, Germany
SOURCE: Tetrahedron: Asymmetry (2003), 14(20), 3141-3152
PUBLISHER: CODEN: TASYE3; ISSN: 0957-4166
DOCUMENT TYPE: Elsevier Science B.V.
LANGUAGE: Journal
OTHER SOURCE(S): English
GI CASREACT 140:5276



AB Starting from natural 4-hydroxyproline, preparation of the four possible stereoisomers of 4-amino- and 4-aminomethyl-substituted prolinol derivs., resp., was accomplished by chemo- and regioselective functional group transformations at the 2- and 4-positions of the pyrrolidine moiety. These building blocks were used as valuable precursors for the preparation of new methoxybenzamide derivs. Dopamine and *serotonin* binding studies involving the subtypes D1, D2long, D2short, D3 and D4 as well as 5-HT1A and 5-HT2, resp., displayed interesting structure activity relationships, especially with respect to the absolute and relative configuration of the test compds. As a complement to the D3 receptor-preferring aminomethylpyrrolidine FAUC 21 (I; prepared by the authors in an earlier work), one of the title compds., (2R,4R)-aminoprolinol derivative II (FAUC 65), was found to preferentially recognize D4 subtype.
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 2, 27

ST prolinol methoxybenzamide deriv prepn dopamine **serotonin**
receptor binding; aminomethylprolinol aminoprolinol deriv prepn
hydroxyproline precursor

IT Dopamine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D1; preparation of methoxybenzamide derivs. of amino/aminomethyl-
substituted prolinols and their binding of dopamine and
serotonin receptors)

IT Dopamine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D1A; preparation of methoxybenzamide derivs. of amino/aminomethyl-
substituted prolinols and their binding of dopamine and
serotonin receptors)

IT Dopamine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D2(long); preparation of methoxybenzamide derivs. of amino/aminomethyl-
substituted prolinols and their binding of dopamine and
serotonin receptors)

IT Dopamine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D2(short); preparation of methoxybenzamide derivs. of amino/aminomethyl-
substituted prolinols and their binding of dopamine and
serotonin receptors)

IT Dopamine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D3; preparation of methoxybenzamide derivs. of amino/aminomethyl-
substituted prolinols and their binding of dopamine and
serotonin receptors)

IT Dopamine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D4; preparation of methoxybenzamide derivs. of amino/aminomethyl-
substituted prolinols and their binding of dopamine and
serotonin receptors)

IT Structure-activity relationship
(dopaminergic receptor-binding; preparation of methoxybenzamide derivs. of
amino/aminomethyl-substituted prolinols and their binding of dopamine
and **serotonin** receptors)

IT Structure-activity relationship
(**serotonergic** receptor-binding; preparation of methoxybenzamide
derivs. of amino/aminomethyl-substituted prolinols and their binding of
dopamine and **serotonin** receptors)

IT 5-HT receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type 5-HT1A; preparation of methoxybenzamide derivs. of
amino/aminomethyl-substituted prolinols and their binding of dopamine
and **serotonin** receptors)

IT 5-HT receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type 5-HT2; preparation of methoxybenzamide derivs. of
amino/aminomethyl-substituted prolinols and their binding of dopamine
and **serotonin** receptors)

IT 15676-16-1, Sulpiride 229322-99-0, FAUC 21
RL: PAC (Pharmacological activity); BIOL (Biological study)
(comparisons of dopamine and **serotonin** receptor-binding
activities)

IT 627100-88-3P 627100-89-4P 627100-90-7P 627100-91-8P
627100-93-0P 627100-95-2P 627100-97-4P
627101-23-9P 627101-24-0P 627101-25-1P 627529-76-4P,
FAUC 65
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL

(Biological study); PREP (Preparation)

(preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and **serotonin** receptors)

IT 51-35-4 24201-13-6 61478-25-9 61694-98-2 107746-25-8

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and **serotonin** receptors)

IT 77449-94-6P 77449-99-1P 114677-02-0P 142292-37-3P 154342-88-8P
 154343-00-7P 171192-72-6P 627100-71-4P 627100-72-5P 627100-73-6P
 627100-74-7P 627100-75-8P 627100-76-9P 627100-77-0P 627100-78-1P
 627100-79-2P 627100-80-5P 627100-81-6P 627100-82-7P 627100-83-8P
 627100-84-9P 627100-85-0P 627100-86-1P 627100-99-6P 627101-01-3P
 627101-07-9P 627101-10-4P 627101-12-6P 627101-14-8P 627101-16-0P
 627101-18-2P 627101-20-6P 627101-22-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and **serotonin** receptors)

IT 627100-87-2P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and **serotonin** receptors)

IT 627100-88-3P 627100-89-4P 627100-93-0P
 627100-97-4P 627101-23-9P 627529-76-4P, FAUC

65

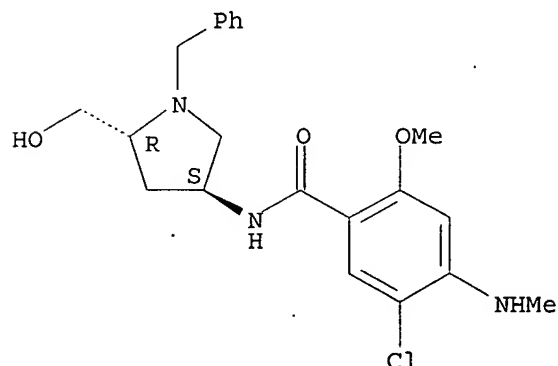
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and **serotonin** receptors)

RN 627100-88-3 CAPLUS

CN Benzamide, 5-chloro-N-[(3S,5R)-5-(hydroxymethyl)-1-(phenylmethyl)-3-pyrrolidinyl]-2-methoxy-4-(methylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 627100-89-4 CAPLUS

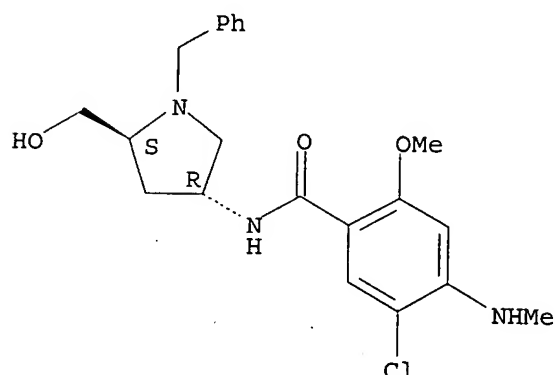
CN Benzamide, 5-chloro-N-[(3S,5S)-5-(hydroxymethyl)-1-(phenylmethyl)-3-pyrrolidinyl]-2-methoxy-4-(methylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

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pyrrolidinyl]-2-methoxy-4-(methylamino)- (9CI) (CA INDEX NAME)

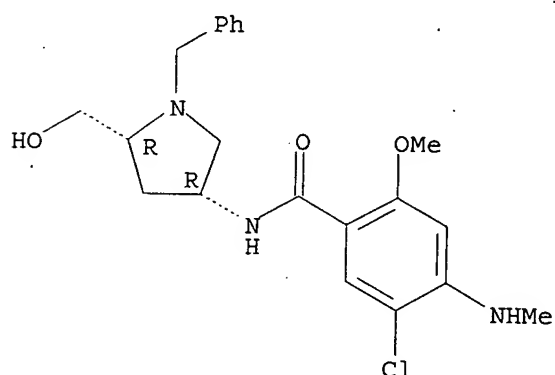
Absolute stereochemistry. Rotation (-).



RN 627529-76-4 CAPLUS

CN Benzamide, 5-chloro-N-[(3R,5R)-5-(hydroxymethyl)-1-(phenylmethyl)-3-pyrrolidinyl]-2-methoxy-4-(methylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 1998:679340 CAPLUS
DOCUMENT NUMBER: 130:47331
TITLE: Effects of **gastrointestinal** prokinetic agents, TKS159 and cisapride, on the in situ canine heart assessed by cardiohemodynamic and electrophysiological monitoring
AUTHOR(S): Sugiyama, Atsushi; Hashimoto, Keitaro
CORPORATE SOURCE: Department of Pharmacology, Yamanashi Medical University, Yamanashi, 409-3898, Japan
SOURCE: Toxicology and Applied Pharmacology (1998), 152(1), 261-269
CODEN: TXAPA9; ISSN: 0041-008X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Effects of a novel 5-HT₄ receptor agonist TKS159 on

the cardiovascular system were assessed in comparison with cisapride using an in vivo canine model. TKS159 in doses of 0.1, 1.0, and 10 mg/kg (n = 6) or cisapride in 1/10 doses of 0.01, 0.1, and 1.0 mg/kg (n = 6) was cumulatively infused over 10 min with a pause of 20 min. The doses of the drugs were determined according to the previous knowledge of their pharmacokinetics. Clin. effective plasma concns. as a **gastrointestinal** prokinetic drug were obtained after the infusion of 0.1 mg/kg of the resp. drugs. In TKS159-administered animals, no significant change was induced in each cardiovascular parameter by an infusion of 0.1 mg/kg. The blood pressure was decreased, and the effective refractory period and repolarization phase of the ventricle were prolonged after 1.0 mg/kg. The heart rate was decreased, and the atrioventricular, as well as intraventricular, conduction were suppressed after 10 mg/kg, while no significant changes were observed in the cardiac output and the ventricular contraction and the relative refractory period of the ventricle during the study. Meanwhile, in cisapride-administered animals, the repolarization phase and the effective refractory period were prolonged after 0.01 mg/kg. The heart rate and the blood pressure were decreased after 0.1 mg/kg. The cardiac output, the ventricular contraction, and the atrioventricular conduction were suppressed, the relative refractory period was prolonged, and early after-depolarization was detected after 1.0 mg/kg, while no significant change was observed in the intraventricular conduction during the study. Thus, TKS159 may have a safer cardiovascular profile than cisapride. (c) 1998 Academic Press.

CC 1-9 (Pharmacology)

IT 5-HT receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(5-HT₄; effects of **gastrointestinal**

prokinetic agent, TKS159, on cardiovascular system in comparison with cisapride)

IT Toxicity

(cardiotoxicity; effects of **gastrointestinal** prokinetic

agent, TKS159, on cardiovascular system in comparison with cisapride)

IT Toxicity

(drug; effects of **gastrointestinal** prokinetic agent, TKS159,

on cardiovascular system in comparison with cisapride)

IT Blood pressure

Cardiovascular system

Heart rate

(effects of **gastrointestinal** prokinetic agent, TKS159, on

cardiovascular system in comparison with cisapride)

IT Heart

(toxicity; effects of **gastrointestinal** prokinetic agent,

TKS159, on cardiovascular system in comparison with cisapride)

IT Cardiac contraction

(ventricular; effects of **gastrointestinal** prokinetic agent,

TKS159, on cardiovascular system in comparison with cisapride)

IT 81098-60-4, Cisapride 142228-17-9, TKS159

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)

(effects of **gastrointestinal** prokinetic agent, TKS159, on

cardiovascular system in comparison with cisapride)

IT 142228-17-9, TKS159

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)

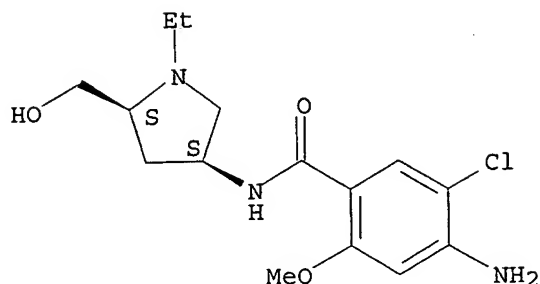
(effects of **gastrointestinal** prokinetic agent, TKS159, on

cardiovascular system in comparison with cisapride)

RN 142228-17-9 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 1996:170355 CAPLUS

DOCUMENT NUMBER: 124:221382

TITLE: Identification of putative 5-hydroxytryptamine4 (5-HT₄) receptors in guinea pig *stomach*: the effect of TKS159, a novel agonist, on *gastric motility* and acetylcholine release

AUTHOR(S): Matsuyama, Shogo; Sakiyama, Hideyo; Nei, Koji; Tanaka, Chikako

CORPORATE SOURCE: Sch. Med., Kobe Univ., Kobe, 650, Japan

SOURCE: Journal of Pharmacology and Experimental Therapeutics (1996), 276(3), 989-95

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors investigated the existence and the function of 5-hydroxytryptamine4 (5-HT₄) receptors and the effect of TKS159, a novel agonist of 5-HT₄ receptor, on guinea pig *stomach*. The mech. activity and the release of [3H]ACh were measured using preps. of muscle layers attached to intramural plexus from guinea pig *stomach*. 5-HT in the presence of 1 μM methysergide, 1 μM ketanserin and 1 μM granisetron, 5-methoxytryptamine or TKS159 enhanced the elec. transmural stimulation-evoked contraction and [3H]ACh release in strips of the *stomach* in a concentration-dependent manner. This enhancement by 5-HT, 5-methoxytryptamine or TKS159 was antagonized by SDZ 205-557 or atropine. Cisapride, metoclopramide and TKS159 enhanced the elec. transmural stimulation-evoked contraction and release of [3H]ACh in a concentration-dependent manner. The authors conclude that the pharmacol. characteristics of the receptor, which mediates contraction of the guinea pig *stomach* by the activation of cholinergic nerves, are consistent with its being of the putative 5-HT₄ receptor type and that TKS159 is an agonist at 5-HT₄ receptors.

CC 2-8 (Mammalian Hormones)

Section cross-reference(s): 1

ST *serotonin* S4 receptor *stomach* acetylcholine; TKS 159 *stomach motility* acetylcholine

IT *Stomach* (*serotonin* S4 receptor characterization in guinea pig *stomach* and TKS 159 effect on *gastric*

motility and acetylcholine release)

IT Receptors
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (serotonergic S4, serotonin S4 receptor
 characterization in guinea pig stomach and TKS 159 effect on
 gastric motility and acetylcholine release)

IT 50-67-9, Serotonin, biological studies 608-07-1,
 5-Methoxytryptamine 142228-17-9, TKS 159
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); BIOL (Biological study)
 (serotonin S4 receptor characterization in guinea pig
 stomach and TKS 159 effect on gastric
 motility and acetylcholine release)

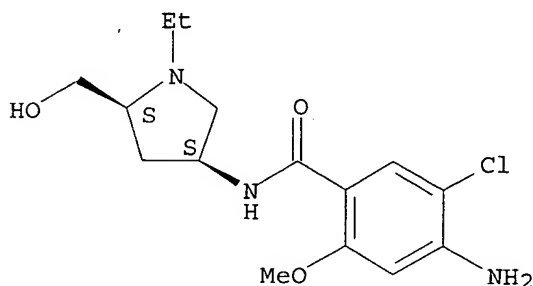
IT 51-84-3, Acetylcholine, biological studies
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (serotonin S4 receptor characterization in guinea pig
 stomach and TKS 159 effect on gastric
 motility and acetylcholine release)

IT 142228-17-9, TKS 159
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); BIOL (Biological study)
 (serotonin S4 receptor characterization in guinea pig
 stomach and TKS 159 effect on gastric
 motility and acetylcholine release)

RN 142228-17-9 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-
 pyrrolidiny]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L86 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1255208 CAPLUS

DOCUMENT NUMBER: 144:150625

TITLE: Design and Synthesis of Photoaffinity-Labeling Ligands
 of the L-Prolyl-L-leucylglycinamide Binding Site
 Involved in the Allosteric Modulation of the Dopamine
 Receptor

AUTHOR(S): Fisher, Abigail; Mann, Amandeep; Verma, Vaneeta;
 Thomas, Nancy; Mishra, Ram K.; Johnson, Rodney L.

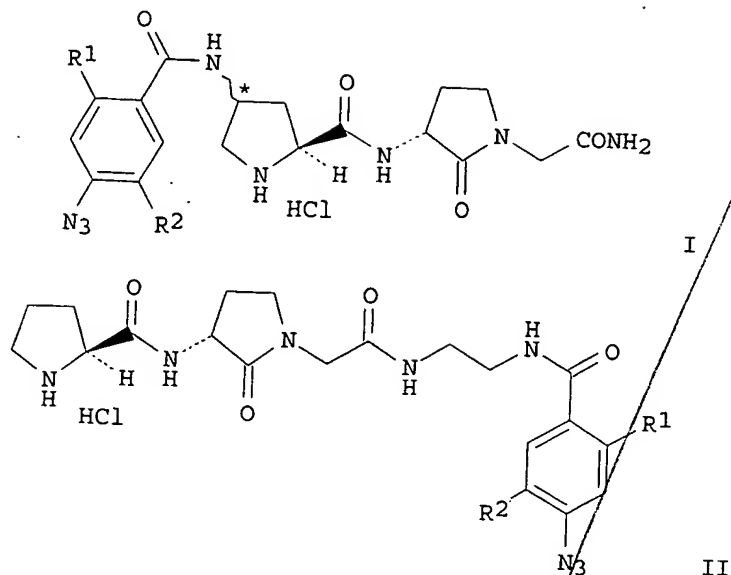
CORPORATE SOURCE: Department of Medicinal Chemistry, University of
 Minnesota, Minneapolis, MN, 55455-0343, USA

SOURCE: Journal of Medicinal Chemistry (2006), 49(1), 307-317
 CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English
 OTHER SOURCE(S): CASREACT 144:150625
 GI



AB Peptide H-Pro-Leu-Gly-NH₂ (PLG), in addition to its endocrine effects, possesses the ability to modulate dopamine D₂ receptors within the central nervous system. However, the precise binding site of PLG is unknown. Potential photoaffinity-labeling ligands of the PLG binding site were designed as tools to be used in the identification of the macromol. that possesses this binding site. Photoaffinity-labeling ligands, PLG peptidomimetics I (both trans and cis diastereomers at *'d locant were obtained) and II, were designed and synthesized. The 4-azidobenzoyl and 4-azido-2-hydroxybenzoyl photoaffinity-labeling moieties were placed at opposite ends of PLG peptidomimetic to generate a series of ligands that potentially could be used to map the PLG binding site. All of the compds. that were synthesized possessed activity comparable to or better than PLG in enhancing [3H]-N-propylnorapomorphine agonist binding to dopamine receptors. Photoaffinity ligands that were cross-linked to the receptor preparation produced a modulatory effect that was either comparable to or greater than the increase in agonist binding produced by the resp. ligands that were not cross-linked to the dopamine receptor. The results indicate that these photoaffinity-labeling agents are binding at the same allosteric site as PLG and PLG peptidomimetics.

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1

IT 874163-12-9P 874163-13-0P 874163-14-1P 874163-15-2P
 874163-16-3P 874163-23-2P 874163-24-3P 874163-25-4P

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);
 BIOL (Biological study); PREP (Preparation)

(preparation and biol. activity of photoaffinity-labeled peptidomimetics of prolylleucylglycinamide to study its binding site involved in allosteric modulation of dopamine receptor)

IT 96602-46-9P 99298-06-3P 185304-19-2P 865295-35-8P 874162-95-5P
 874162-96-6P 874162-97-7P 874162-98-8P 874162-99-9P 874163-00-5P
 874163-02-7P 874163-03-8P 874163-04-9P 874163-05-0P 874163-06-1P
 874163-07-2P 874163-08-3P 874163-09-4P 874163-10-7P

874163-11-8P 874163-18-5P 874163-19-6P 874163-20-9P
874163-21-0P 874163-22-1P 874163-26-5P 877262-55-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation and biol. activity of photoaffinity-labeled peptidomimetics of
prolylleucylglycinamide to study its binding site involved in
allosteric modulation of dopamine receptor)

IT 874163-17-4P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and biol. activity of photoaffinity-labeled peptidomimetics of
prolylleucylglycinamide to study its binding site involved in
allosteric modulation of dopamine receptor)

IT 874163-14-1P

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);

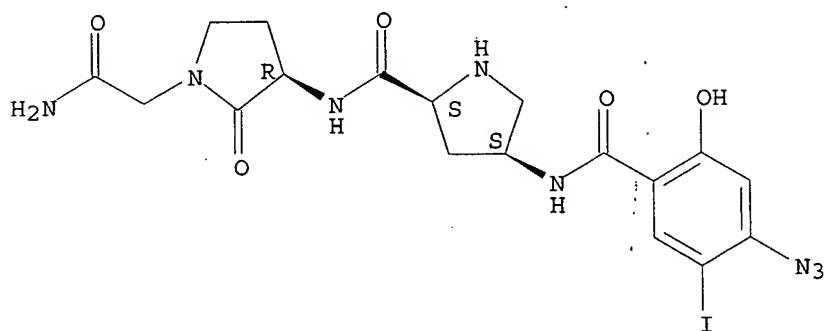
BIOL (Biological study); PREP (Preparation)

(preparation and biol. activity of photoaffinity-labeled peptidomimetics of
prolylleucylglycinamide to study its binding site involved in
allosteric modulation of dopamine receptor)

RN 874163-14-1 CAPLUS

CN 1-Pyrrolidineacetamide, 3-[[[(2S,4S)-4-[(4-azido-2-hydroxy-5-
iodobenzoyl)amino]-2-pyrrolidinyl]carbonyl]amino]-2-oxo-,
monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

IT 874163-08-3P 874163-11-8P

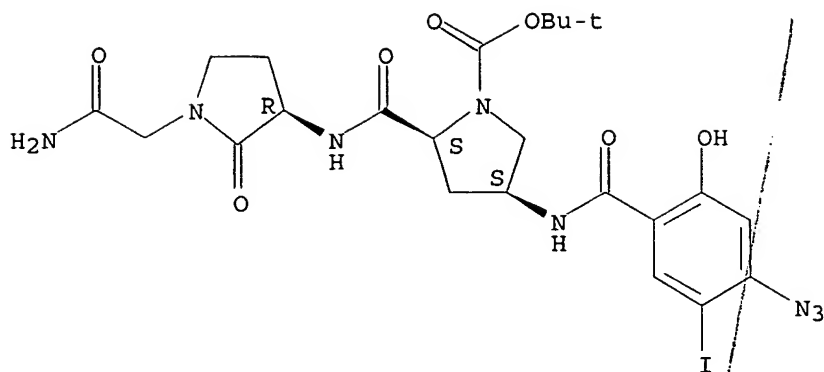
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation and biol. activity of photoaffinity-labeled peptidomimetics of
prolylleucylglycinamide to study its binding site involved in
allosteric modulation of dopamine receptor)

RN 874163-08-3 CAPLUS

CN 1-Pyrrolidinecarboxylic acid, 2-[[[(3R)-1-(2-amino-2-oxoethyl)-2-oxo-3-
pyrrolidinyl]amino]carbonyl]-4-[[4-azido-2-hydroxy-5-iodobenzoyl]amino]-,
1,1-dimethylethyl ester, (2S,4S) (9CI) (CA INDEX NAME)

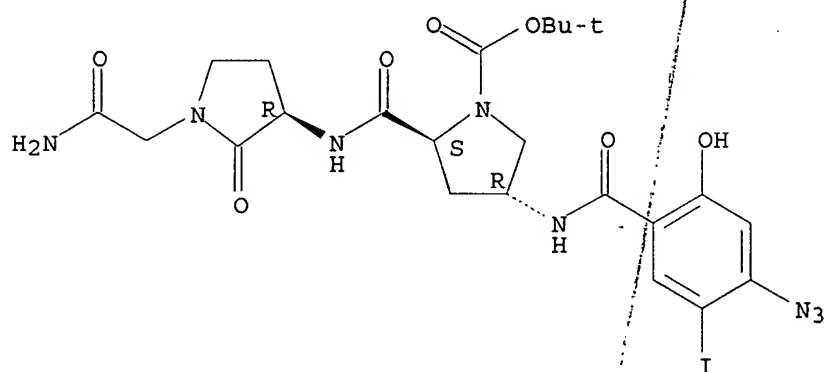
Absolute stereochemistry.



RN 874163-11-8 CAPLUS

CN 1-Pyrrolidinecarboxylic acid, 2-[[[(3R)-1-(2-amino-2-oxoethyl)-2-oxo-3-pyrrolidinyl]amino]carbonyl]-4-[(4-azido-2-hydroxy-5-iodobenzoyl)amino]-, 1,1-dimethylethyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 874163-17-4P

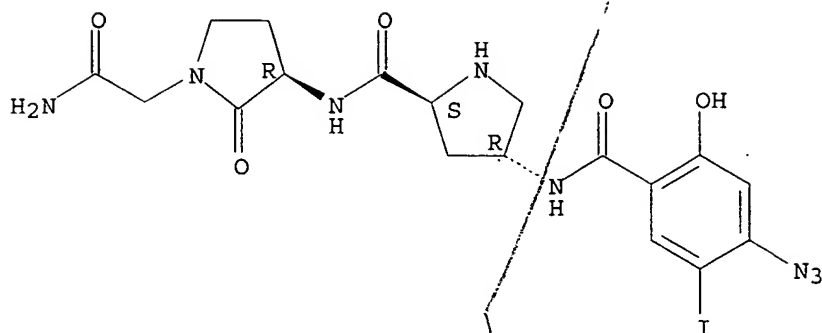
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and biol. activity of photoaffinity-labeled peptidomimetics of prolylleucylglycinamide to study its binding site involved in allosteric modulation of dopamine receptor)

RN 874163-17-4 CAPLUS

CN 1-Pyrrolidineacetamide, 3-[[[(2S,4R)-4-[(4-azido-2-hydroxy-5-iodobenzoyl)amino]-2-pyrrolidinyl]carbonyl]amino]-2-oxo-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/27/2006



● HCl

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1311545 CAPLUS

DOCUMENT NUMBER: 144:51586

TITLE: Preparation of acetamide derivatives as reverse transcriptase inhibitors for treatment of HIV

INVENTOR(S): Deroy, Patrick; Faucher, Anne-Marie; Gagnon, Alexandre; Landry, Serge; Morin, Sebastien; O'Meara, Jeffrey; Simoneau, Bruno; Thavonekham, Bounkham; Yoakim, Christiane

PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany; Boehringer Ingelheim Pharma GmbH & Co KG

SOURCE: PCT Int. Appl., 206 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

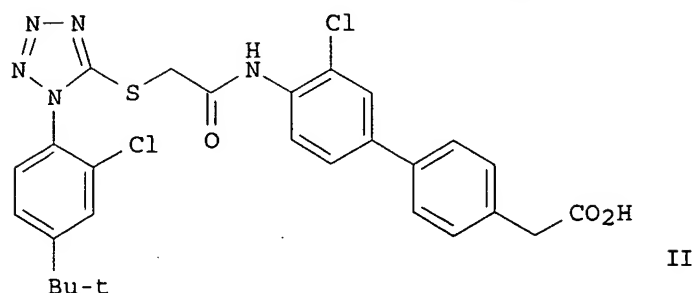
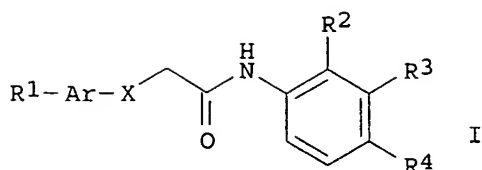
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005118575	A1	20051215	WO 2005-CA907	20050530
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005282907	A1	20051222	US 2005-137831	20050524
CA 2555633	AA	20051215	CA 2005-2555633	20050530
PRIORITY APPLN. INFO.:			US 2004-575888P	P 20040601
			WO 2005-CA907	W 20050530

OTHER SOURCE(S): MARPAT 144:51586

GI



AB The title compds. I [wherein Ar = (un)substituted 5-membered aromatic heterocycle; X = O or S; R1 = (un)substituted Ph; R2 = halo, NO₂, or alkyl; R3 = H or halo; R4 = (un)substituted Ph, alkenyl, heteroaryl, etc.] or enantiomers, diastereomers, tautomers, or pharmaceutically acceptable salts thereof were prepared as reverse transcriptase inhibitors against wild type and single or double mutant strains of HIV for the treatment or prophylaxis of HIV infection. For example, the compound II was prepared in a multi-step synthesis. The enzymic assay was conducted.

IC ICM C07D403-12

ICS A61K031-41; A61K031-4439; A61K031-454; A61K031-4709; A61K031-495; A61K031-5377; A61K031-541; A61P031-18; C07D257-04; C07D249-04; C07D249-10; C07D277-36; C07D285-06

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

IT 871473-75-5P	871473-76-6P	871473-77-7P	871473-78-8P	871473-79-9P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of acetamide derivs. as reverse transcriptase inhibitors for treatment of HIV infection)

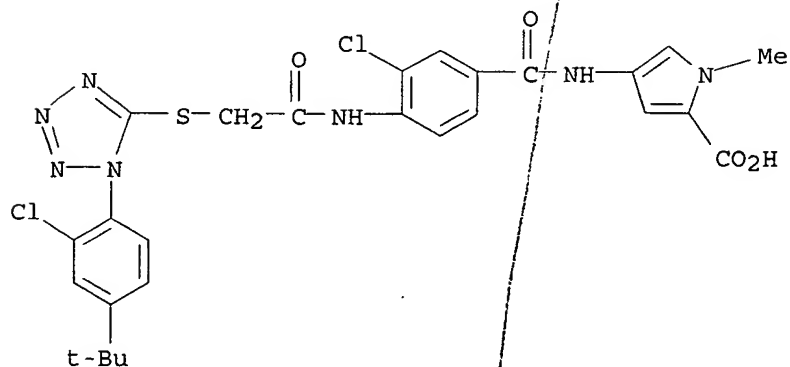
IT 871475-96-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of acetamide derivs. as reverse transcriptase inhibitors for treatment of HIV infection)

RN 871475-96-6 CAPLUS

CN 1H-Pyrrole-2-carboxylic acid, 4-[[[3-chloro-4-[[[1-[2-chloro-4-(1,1-dimethylethyl)phenyl]-1H-tetrazol-5-yl]thio]acetyl]amino]benzoyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:813105 CAPLUS
 DOCUMENT NUMBER: 142:221
 TITLE: Hybridized particle swarm algorithm for adaptive structure training of multilayer feed-forward neural network: QSAR studies of bioactivity of organic compounds
 AUTHOR(S): Shen, Qi; Jiang, Jian-Hui; Jiao, Chen-Xu; Lin, Wei-Qi; Shen, Guo-Li; Yu, Ru-Qin
 CORPORATE SOURCE: State Key Laboratory of Chemo/Biosensing and Chemometrics, College of Chemistry and Chemical Engineering, Hunan University, Changsha, 410082, Peop. Rep. China
 SOURCE: Journal of Computational Chemistry (2004), 25(14), 1726-1735
 CODEN: JCCHDD; ISSN: 0192-8651
 PUBLISHER: John Wiley & Sons, Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The multilayer feed-forward ANN is an important modeling technique used in QSAR studying. The training of ANN is usually carried out only to optimize the wts. of the neural network and without paying attention to the network topol. Some other strategies used to train ANN are, first, to discover an optimum structure of the network, and then to find wts. for an already defined structure. These methods tend to converge to local optima, and may also lead to overfitting. In this article, a hybridized particle swarm optimization (PSO) approach was applied to the neural network structure training (HPSONN). The continuous version of PSO was used for the weight training of ANN, and the modified discrete PSO was applied to find appropriate the network architecture. The network structure and connectivity are trained simultaneously. The two versions of PSO can jointly search the global optimal ANN architecture and wts. A new objective function is formulated to determine the appropriate network architecture and optimum value of the wts. The proposed HPSONN algorithm was used to predict carcinogenic potency of aromatic amines and biol. activity of a series of distamycin and distamycin-like derivs. The results were compared to those obtained by PSO and GA training in which the network architecture was kept fixed. The comparison demonstrated that the HPSONN is a useful tool for training ANN, which converges quickly towards the optimal position, and can avoid overfitting in some extent.

CC 1-3 (Pharmacology)

IT	6576-51-8	118438-45-2	132244-47-4	132268-26-9	132268-27-0
	177409-19-7	177409-26-6	177409-27-7	177409-30-2	177409-42-6
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	797060-07-2				

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(hybridized particle swarm algorithm for adaptive structure training of multilayer feed-forward neural network and QSAR studies of bioactivity of organic compds.)

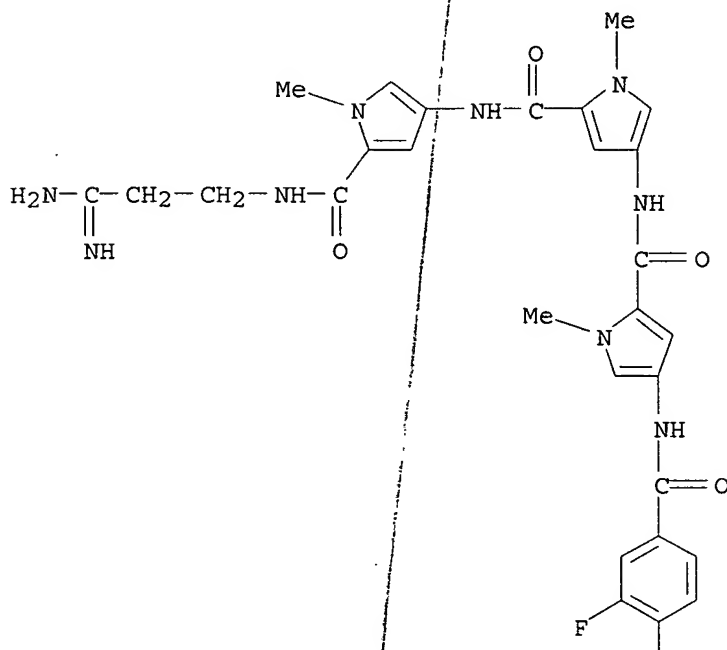
IT 203118-15-4

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (hybridized particle swarm algorithm for adaptive structure training of multilayer feed-forward neural network and QSAR studies of bioactivity of organic compds.)

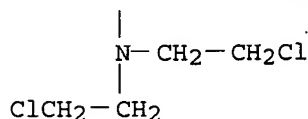
RN 203118-15-4 CAPLUS

CN 1H-Pyrrole-2-carboxamide, N-[5-[[[(3-amino-3-iminopropyl)amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-4-[[[4-[[4-[bis(2-chloroethyl)amino]-3-fluorobenzoyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



● HCl

REFERENCE COUNT:

20

THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:353274 CAPLUS

DOCUMENT NUMBER: 136:363862

TITLE: Composition comprising: *serotonin* receptor antagonists (5HT-2, 5HT-3) and agonist (5HT-4)
 INVENTOR(S): Skogvall, Staffan
 PATENT ASSIGNEE(S): Respiratorius A.B., Swed.
 SOURCE: PCT Int. Appl., 160 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002036113	A1	20020510	WO 2001-SE2372	20011030
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, FR, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, VZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002012888	A5	20020515	AU 2002-12888	20011030
PRIORITY APPLN. INFO.: SE 2000-3995 A 20001101 US 2000-244661P P 20001101 WO 2001-SE2372 W 20011030				
AB A composition comprising a combination of (a) at least one compound with agonist activity to the 5-HT ₄ receptor, (b) at least one compound with antagonist activity to the 5-HT ₃ receptor, and (c) at least one compound with antagonist activity to the 5-HT ₂ receptor is described. The invention relates to the use of said composition as a medicament for therapeutic or prophylactic treatment of disorders involving airway constriction in humans or animals.				
IC	ICM A61K031-395 ICS A61K031-4045; A61P011-06; A61P011-08			
CC	1-11 (Pharmacology)			
ST	<i>serotonin</i> receptor agonist antagonist airway constriction treatment			
IT	5-HT antagonists (5-HT ₂ ; composition comprising 5-HT ₂ and 5-HT ₃ <i>serotonin</i> receptor antagonists and 5-HT ₄ agonist as medicament for treatment of disorders involving airway constriction)			
IT	5-HT antagonists (5-HT ₃ ; composition comprising 5-HT ₂ and 5-HT ₃ <i>serotonin</i> receptor antagonists and 5-HT ₄ agonist as medicament for treatment of disorders involving airway constriction)			
IT	5-HT agonists (5-HT ₄ ; composition comprising 5-HT ₂ and 5-HT ₃ <i>serotonin</i> receptor antagonists and 5-HT ₄ agonist as medicament for treatment of disorders involving airway constriction)			
IT	Bronchi, disease Inflammation (chronic bronchitis; composition comprising 5-HT ₂ and			

- 5-*HT3* serotonin receptor antagonists and 5-*HT4* agonist as medicament for treatment of disorders involving airway constriction)
- IT Lung, disease
(chronic obstructive pulmonary disease; composition comprising 5-*HT2* and 5-*HT3* serotonin receptor antagonists and 5-*HT4* agonist as medicament for treatment of disorders involving airway constriction)
- IT Antiasthmatics
Drug interactions
Emphysema
(composition comprising 5-*HT2* and 5-*HT3* serotonin receptor antagonists and 5-*HT4* agonist as medicament for treatment of disorders involving airway constriction)
- IT 5-*HT* receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type 5-*HT2*; composition comprising 5-*HT2* and 5-*HT3* serotonin receptor antagonists and 5-*HT4* agonist as medicament for treatment of disorders involving airway constriction)
- IT 5-*HT* receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type 5-*HT3*; composition comprising 5-*HT2* and 5-*HT3* serotonin receptor antagonists and 5-*HT4* agonist as medicament for treatment of disorders involving airway constriction)
- IT 5-*HT* receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type 5-*HT4*; composition comprising 5-*HT2* and 5-*HT3* serotonin receptor antagonists and 5-*HT4* agonist as medicament for treatment of disorders involving airway constriction)
- IT 138559-58-7, ADR 932
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ADR 932; composition comprising 5-*HT2* and 5-*HT3* serotonin receptor antagonists and 5-*HT4* agonist as medicament for treatment of disorders involving airway constriction)
- IT 178485-02-4, ALEPH 2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALEPH 2; composition comprising 5-*HT2* and 5-*HT3* serotonin receptor antagonists and 5-*HT4* agonist as medicament for treatment of disorders involving airway constriction)
- IT 150527-36-9, FG 5974
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(FG 5974; composition comprising 5-*HT2* and 5-*HT3* serotonin receptor antagonists and 5-*HT4* agonist as medicament for treatment of disorders involving airway constriction)
- IT 116684-57-2, GR 67330
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GR 67330; composition comprising 5-*HT2* and 5-*HT3* serotonin receptor antagonists and 5-*HT4* agonist as medicament for treatment of disorders involving

airway constriction)

IT 148014-93-1, KB 6933
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (KB 6933; composition comprising 5-HT2 and 5-HT3 serotonin receptor antagonists and 5-HT4 agonist as medicament for treatment of disorders involving airway constriction)

IT 145970-12-3, KF 20170
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (KF 20170; composition comprising 5-HT2 and 5-HT3 serotonin receptor antagonists and 5-HT4 agonist as medicament for treatment of disorders involving airway constriction)

IT 153415-44-2, LEK 8804
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (LEK 8804; composition comprising 5-HT2 and 5-HT3 serotonin receptor antagonists and 5-HT4 agonist as medicament for treatment of disorders involving airway constriction)

IT 107007-94-3, LY 211000
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (LY 211000; composition comprising 5-HT2 and 5-HT3 serotonin receptor antagonists and 5-HT4 agonist as medicament for treatment of disorders involving airway constriction)

IT 143257-98-1, Lerisetron
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (Lerisetron; composition comprising 5-HT2 and 5-HT3 serotonin receptor antagonists and 5-HT4 agonist as medicament for treatment of disorders involving airway constriction)

IT 160472-97-9, N 3389
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (N 3389; composition comprising 5-HT2 and 5-HT3 serotonin receptor antagonists and 5-HT4 agonist as medicament for treatment of disorders involving airway constriction)

IT 161362-69-2, RS 67532
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (RS 67532; composition comprising 5-HT2 and 5-HT3 serotonin receptor antagonists and 5-HT4 agonist as medicament for treatment of disorders involving airway constriction)

IT 175413-81-7, SB 205149
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (SB 205149; composition comprising 5-HT2 and 5-HT3 serotonin receptor antagonists and 5-HT4 agonist as medicament for treatment of disorders involving airway constriction)

IT 169789-38-2, SDZ 216-454
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(SDZ 216-454; composition comprising 5-HT₂ and 5-HT₃ serotonin receptor antagonists and 5-HT₄ agonist as medicament for treatment of disorders involving airway constriction)

IT 148611-75-0, WAY-SEC 579
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (WAY-SEC 579; composition comprising 5-HT₂ and 5-HT₃ serotonin receptor antagonists and 5-HT₄ agonist as medicament for treatment of disorders involving airway constriction)

IT 21867-64-1
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (aryl derivs.; composition comprising 5-HT₂ and 5-HT₃ serotonin receptor antagonists and 5-HT₄ agonist as medicament for treatment of disorders involving airway constriction)

IT 50-37-3, LSD 50-48-6, Amitriptyline 50-49-7, Imipramine 50-52-2, Thioridazine 50-53-3, Chlorpromazine, biological studies 50-67-9, 5-HT, biological studies 55-45-8 58-38-8, Prochlorperazine 58-39-9, Perphenazine 60-87-7, Promethazine 69-23-8, Fluphenazine 84-02-6, Stemetil 91-84-9, Mepyramine 93-65-2, MCPP 102-02-3, Phenylbiguanide 117-89-5, Trifluoperazine 129-03-3, Cyproheptadine 304-52-9 361-37-5, 364-62-5, Metoclopramide 486-74-8D, Quinoline-4-carboxylic acid, derivs. 487-93-4, Bufotenine 510-74-7, AMI-193 548-43-6, Elymoclavine 548-73-2, Droperidol 608-07-1, 5-Methoxytryptamine 749-02-0, Spiperone 1019-45-0 1166-34-3, Cinanserin 1977-10-2, Loxapine 2851-12-9D, derivs. 3040-44-6D, 1-Piperidineethanol, arylcarbamate derivs. 3546-03-0, Cyamemazine 4205-90-7, Clonidine 4774-24-7, Quipazine 5560-72-5, Iprindole 5786-21-0 6104-71-8, N-Desmethyldiazepam 6480-67-7D, Quinoline-3-carboxamide, derivs. 7206-70-4D, derivs. 7206-70-4D, 4-Amino-5-chloro-2-methoxybenzoic acid, esters 15532-75-9, TFMPP 15574-96-6, Pizotifen 15676-16-1, Sulpiride 16357-59-8, N-Ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline 17692-51-2, Metergoline 20980-22-7D, 1-(2-Pyrimidinyl)piperazine, derivs. 21236-55-5, QX 222 23210-56-2, Ifenprodil 24190-74-7D, derivs. 24219-97-4, Mianserin 28614-26-8, N-Methylquipazine 31363-74-3, 5,7-Dihydroxytryptamine 32359-34-5, Medifoxamine 39133-31-8, Trimebutine 39478-62-1 40796-97-2, Bemisetron 42399-41-7, Diltiazem 43135-91-7D, Benzimidazolone, derivs. 54504-71-1, ML-1035 54739-18-3, Fluvoxamine 54910-89-3, Fluoxetine 55905-53-8, Clebopride 57260-68-1D, derivs. 57818-92-5, TMB 8 59729-33-8, Citalopram 60634-51-7, LY 53857 61869-08-7, Paroxetine 63758-79-2, Indalpine 64022-27-1, MK 212 64097-94-5 64795-35-3, Mesulergine 66564-14-5, Cinitapride 68696-79-7D, derivs. 74050-98-9, Ketanserin 74885-09-9 75272-39-8, YM-09151 75444-65-4, Pirenperone 75558-90-6, Amperozide 76272-78-1, BRL 24682 78263-90-8, 2-Methylserotonin 78950-78-4, 8-Hydroxy-2-dipropylaminotetralin 79617-96-2; Sertraline 81098-60-4, Cisapride 83366-66-9, Nefazodone 84225-95-6, Raclopride 84625-59-2, Dotarizine 85273-96-7, ICI 169369 85650-52-8, Mirtazapine 86811-09-8, Litoxetine 87051-43-2, Ritanerlin 89565-68-4, Tropisetron 89565-96-8, SDZ 206-830 89771-28-8, SDZ 206-792 90182-92-6, Zacopride 99390-76-8, BRL 20627 99444-89-0, SDZ 210-204 99614-01-4, GR 38032F 99614-02-5, Ondansetron 99746-68-6, (R,R)-LY-53857 99746-70-0, (S,R)-LY-53857 99746-72-2, (R,S)-LY-53857 100648-19-9, RU 28253 100746-36-9, CGS 18102A 100762-72-9, (S,S)-LY-53857 101626-70-4, Talipexole 102670-46-2, Batanopride 106243-16-7, Thioperamide 106266-06-2, Risperidone 106469-51-6, BIM 107008-28-6, RU 24969

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 112727-80-7, Renzapride 112885-41-3, Mosapride 112922-55-1,
 Cericlamine 113140-33-3, GR 65630 115338-32-4, NAN-190 115626-53-4,
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 115956-13-3, Dolasetron mesylate 116684-92-5, Galdanetron
 117086-68-7, BRL 46470 120357-05-3 120444-71-5, Deramciclane
 120635-74-7, Cilansetron 120713-18-0, BMV 33462 121588-75-8,
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 129299-90-7, FK 1052 130580-02-8, SR 46349B 131012-61-8 132036-88-5,
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 BIMU 8 134401-97-1D, 2,3-Dihydrobenzofuran-7-carboxamide, derivs.
 135729-55-4, RS 42358-197 135729-61-2, Palonosetron 135905-89-4,
 Mirisetron 136013-69-9, WAY 100289 136174-04-4, RG 12915
 136861-96-6, MDL 28133A 137328-52-0, LY 215840 138752-34-8, RS 56532
 139094-48-7, KF 18259 139290-65-6, MDL 100907 139290-69-0, MDL 100151
 140865-88-9, BRL 46470A 141034-42-6, DAT 582 141196-99-8, SC-53116
 141533-35-9, SDZ 216-525 142228-17-9, TKS 159 143137-35-3, RS
 56812 143137-37-5, RS-056812-198 143178-84-1, MDL 72699 143381-68-4,
 ADR-882 143407-29-8, Iodophenpropit 144625-51-4, GR 113808
 145082-87-7, KF 17643 146388-57-0, SC-49518 146714-97-8, WAY 100635
 146715-07-3, Desmethy-WAY 100635 147600-74-6, SC-52491 148565-09-7,
 KB-R 6933 148702-58-3, SB 204070 148868-55-7, ML 10302 149409-57-4,
 NE-100 149685-78-9 149685-89-2 149719-06-2, RS 23597 153608-99-2,
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 162413-52-7, GK 128 166743-12-0, SK-951 166815-18-5, RS 17017
 167933-07-5, BIMT 17 168986-60-5, RS 67333 168986-61-6, RS 67506
 172679-55-9, SR 59768 173339-89-4, Y-34959 179474-81-8, Prucalopride
 179913-42-9 182808-16-8D, derivs. 183949-64-6, NRA0045 193404-36-3,
 RS 57639 202590-69-0, (+)-Norcisapride 202590-69-0D, derivs.
 207605-20-7 208661-17-0, LU 111995 217635-62-6 217635-64-8
 220850-98-6, YM-53389 303953-05-1 303953-06-2 303955-07-9, YM-47813
 380847-59-6D, derivs. 380847-60-9D, derivs. 380847-61-0D, derivs.
 380847-66-5 380893-13-0, BRL 47204 380893-14-1, CP-93318
 380893-15-2, GYKI-48903 380893-16-3, KB-6922 380893-18-5, N-3256
 380893-19-6, ONO-3051 380893-20-9, RS-25259 380893-21-0, SDZ 210-205
 380893-22-1, SDZ 214-322 380893-23-2, SDZ 322 380893-25-4, Y 2513

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(composition comprising 5-HT₂ and 5-

HT₃ serotonin receptor antagonists and 5-

HT₄ agonist as medicament for treatment of disorders involving
 airway constriction)

IT 380893-26-5, SEC 579 422506-75-0D, derivs. 422506-76-1D, derivs.

422506-77-2 422509-62-4D, derivs.

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(composition comprising 5-HT₂ and 5-

HT₃ serotonin receptor antagonists and 5-

HT₄ agonist as medicament for treatment of disorders involving
 airway constriction)

IT 142228-17-9, TKS 159

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

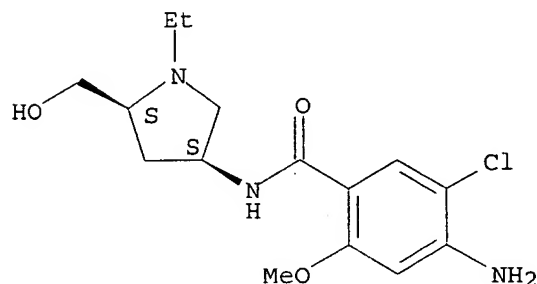
10/27/2006

(composition comprising 5-HT2 and 5-HT3 serotonin receptor antagonists and 5-HT4 agonist as medicament for treatment of disorders involving airway constriction)

RN 142228-17-9 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidiny]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:923608 CAPLUS

DOCUMENT NUMBER: 136:31700

TITLE: A composition comprising a combination of 5-HT4 receptor agonists and 5-HT3 receptor antagonists for treatment of disorders involving airway constriction

INVENTOR(S): Skogvall, Staffan

PATENT ASSIGNEE(S): Respiratorius AB, Swed.

SOURCE: PCT Int. Appl., 149 pp.

CODEN: PIXAD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001095902	A1	20011220	WO 2000-SE2612	20001220
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 2001025663	A5	20011224	AU 2001-25663	20001220
EP 1302204	A1	20030416	EP 2001-610108	20011015
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			

PRIORITY APPLN. INFO.: SE 2000-1267 A 20000615
WO 2000-SE1267 A 20000615
WO 2000-SE2612 W 20001220

AB The present invention relates to a composition comprising a combination of (a) at least one compound with agonist activity to the 5-HT4

receptor and (b) at least one compound with antagonist activity to the 5-HT₃ receptor and to the use of said compound in the manufacture of a medicament for therapeutic or prophylactic treatment of disorders involving airway constriction of a human or animal body, as well as methods of treatment, wherein said compds. are administered.

IC A61K031-395; A61K031-4045; A61P011-06; A61P011-08

CC 1-9 (Pharmacology)

ST airway constriction disorder HT receptor agonist antagonist; serotonin receptor agonist antagonist airway constriction disorder

IT 5-HT antagonists
 (5-HT₃; composition comprising a combination of 5-HT₄ receptor agonists and 5-HT₃ receptor antagonists for treatment of disorders involving airway constriction)

IT 5-HT agonists
 (5-HT₄; composition comprising a combination of 5-HT₄ receptor agonists and 5-HT₃ receptor antagonists for treatment of disorders involving airway constriction)

IT Bronchodilators
 Drug interactions
 (composition comprising a combination of 5-HT₄ receptor agonists and 5-HT₃ receptor antagonists for treatment of disorders involving airway constriction)

IT Respiratory system, disease
 (pathol. constriction; composition comprising a combination of 5-HT₄ receptor agonists and 5-HT₃ receptor antagonists for treatment of disorders involving airway constriction)

IT Muscle relaxants
 (smooth; composition comprising a combination of 5-HT₄ receptor agonists and 5-HT₃ receptor antagonists for treatment of disorders involving airway constriction)

IT 5-HT receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (type 5-HT₃; composition comprising a combination of 5-HT₄ receptor agonists and 5-HT₃ receptor antagonists for treatment of disorders involving airway constriction)

IT 5-HT receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (type 5-HT₄; composition comprising a combination of 5-HT₄ receptor agonists and 5-HT₃ receptor antagonists for treatment of disorders involving airway constriction)

IT 148014-93-1, KB 6933
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (KB 6933; composition comprising a combination of 5-HT₄ receptor agonists and 5-HT₃ receptor antagonists for treatment of disorders involving airway constriction)

IT 107007-94-3, LY 211000
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (LY 211000; composition comprising a combination of 5-HT₄ receptor agonists and 5-HT₃ receptor antagonists for treatment of disorders involving airway constriction)

IT 169789-38-2, SDZ 216-454
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (SDZ 216-454; composition comprising a combination of 5-

HT4 receptor agonists and 5-HT3 receptor antagonists for treatment of disorders involving airway constriction)
 IT 50-48-6, Amitriptyline 50-49-7, Imipramine 50-53-3, Chlorpromazine, biological studies 50-67-9, **Serotonin**, biological studies 51-17-2D, Benzimidazole, 2-piperidinomethyl ethers 55-45-8 58-38-8, Prochlorperazine 58-39-9, Perphenazine 69-23-8, Fluphenazine 91-84-9, Mepyramine 93-65-2, MCPP 102-02-3, Phenylbiguanide 117-89-5, Trifluoperazine 129-03-3, Cyproheptadine 304-52-9 361-37-5 364-62-5, Metoclopramide 480-91-1D, derivs. 487-93-4, Bufotenine 548-73-2, Droperidol 608-07-1, 5-Methoxytryptamine 3040-44-6D, 1-Piperidine ethanol, arylcarbamate derivs. 3546-03-0, Cyamemazine 4774-24-7, Quipazine 5786-21-0 7206-70-4D, derivs. 7206-70-4D, 4-Amino-5-chloro-2-methoxybenzoic acid, esters 15532-75-9, TFMPP 15574-96-6, Pizotifen 17692-51-2, Metergoline 21236-55-5, QX 222 23210-56-2, Ifenprodil 24190-74-7D, 4-Amino-5-chloro-2-methoxy benzamide, derivs. 24219-97-4, Mianserin 28614-26-8, N-Methylquipazine 39133-31-8, Trimebutine 39478-62-1 40796-97-2, MDL 72222 42399-41-7, Diltiazem 54504-71-1, ML-1035 55745-83-0D, derivs. 55905-53-8, Clebopride 57818-92-5, TMB 8 63758-79-2, Indalpine 64022-27-1, MK 212 64097-94-5 66564-14-5, Cinitapride 68696-79-7D, derivs. 74050-98-9, Ketanserin 74885-09-9, 5-Carboxamidotryptamine 75272-39-8, YM-09151 76272-78-1, BRL 24682 78263-90-8, 2-Methylserotonin 78950-78-4, 8-Hydroxy-2-dipropylaminotetralin 81098-60-4, Cisapride 85650-52-8, Mirtazapine 86811-09-8, Litoxetine 87051-43-2, Ritanserin 89565-68-4, ICS 205930 89565-96-8, SDZ 206-830 89771-28-8, SDZ 206-792 90182-92-6, Zalcopride 98330-05-3, Anpirtoline 99390-76-8, BRL 20627 99444-89-0, SDZ 210-204 99614-01-4, GR 38032F 99614-02-5, Ondansetron 100648-19-9, RU 28253 101626-70-4, Talipexole 102670-46-2, Batanopride 106243-16-7, Thioperamide 106469-51-6, CF 109203 107008-28-6, RU 24969 109216-57-1, LY 258458 109216-58-2, LY 278584 109216-59-3, LY 278989 109872-41-5, BRL 24924 109889-09-0, BRL 43694 111628-39-8D, derivs. 112727-80-7, Renzapride 112885-41-3, Mosapride 113140-33-3, GR 65630 115338-32-4, NAN-190 115626-53-4, QICS 205-930 115753-79-2, Galanolactone 115956-12-2, Dolasetron 115956-13-3, Dolasetron mesylate 116356-96-8D, Thiophene carboxamide, derivs. 116684-57-2, GR 67330 116684-92-5, Galdansetron 117086-68-7, BRL 46470 120635-74-7, Cilansetron 120713-18-0, BMJ 33462 121650-80-4, Pancopride 122852-42-0, Alosetron 122866-79-9, R076186 123040-69-7, Azasetron 123258-84-4, Itasetron 123441-85-0, (R)-Zalcopride 123482-22-4, Zatosetron 123805-17-4, ADR 851 127595-11-3, DAU 6236 127595-43-1, BIMU 1 127618-28-4, DAU 6215 127625-29-0, RP 62203 128200-30-6, L-683877 128292-55-7, (-)-Zalcopride 128486-54-4, Lurosetron 129295-19-8, AS-5370 129299-90-7, FK 1052 131012-61-8 132036-88-5, Ramosetron 134296-40-5, BIMU 8 135729-55-4, RS 42358-197 135729-61-2, Palonosetron 135729-62-3, RS-25259-197 135905-89-4, Mirisetron 136013-69-9, WAY 100289 136174-04-4, RG 12915 138559-58-7, ADR 932 138682-46-9D, derivs. 138752-34-8, RS 56532 139094-48-7, KF 18259 140865-88-9, BRL 46470A 141034-42-6, DAT 582 141196-99-8, SC-53116 141533-35-9, SDZ 216-525 142228-17-9, TKS 159 143137-35-3, RS 56812 143137-37-5, RS 056812-198 143178-84-1, MDL 72699 143257-98-1, Lerisetron 143381-68-4, ADR-882 143407-29-8, Iodophenpropit 144625-51-4, GR 113808 145082-87-7, KF 17643 145970-12-3 146388-57-0, SC-49518 147600-74-6, SC-52491 148565-09-7, KB-R 6933 148611-75-0, WAY-SEC 579 148702-58-3, SB 204070 148868-55-7, ML-10302 149685-78-9 149685-89-2 149719-06-2, RS 23597 153608-99-2, YM 114 155106-73-3, VB20B7 160472-97-9, N 3389 160599-89-3 161362-69-2, RS 67532 162413-52-7, GK 128 166743-12-0, SK-951 166815-18-5, RS 17017 168986-60-5, RS 67333 168986-61-6, RS 67506 172679-55-9, SR 59768 173339-89-4 174486-91-0D, derivs. 175413-81-7, SB 205149 179474-81-8, Prucalopride 179913-42-9

10/27/2006

182808-16-8D, derivs. 189188-57-6, Zelmac 193404-36-3, RS 57639
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380847-61-0D, derivs. 380847-63-2 380847-64-3 380847-65-4
380847-66-5 380893-13-0, BRL 47204 380893-14-1, CP 93318
380893-15-2, GYKI 48903 380893-16-3, KB 6922 380893-18-5, N 3256
380893-19-6, ONO 3051 380893-20-9, RS 25259 380893-21-0, SDZ 210-205
380893-22-1, SDZ 214-322 380893-23-2, SDZ 322 380893-25-4, Y 2513
380893-26-5, SEC 579

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(composition comprising a combination of 5-HT₄ receptor
agonists and 5-HT₃ receptor antagonists for
treatment of disorders involving airway constriction)

IT 142228-17-9, TKS 159

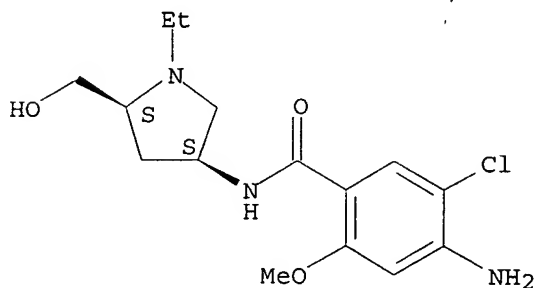
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(composition comprising a combination of 5-HT₄ receptor
agonists and 5-HT₃ receptor antagonists for
treatment of disorders involving airway constriction)

RN 142228-17-9 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-
pyrrolidiny]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:900443 CAPLUS

DOCUMENT NUMBER: 134:51395

TITLE: 5-HT₄ receptor agonists and
5-HT₃ receptor antagonists for
treatment of bronchocontraction

INVENTOR(S): Skogvall, Staffan

PATENT ASSIGNEE(S): Respiratorius Ab, Swed.

SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076500	A2	20001221	WO 2000-SE1267	20000615
WO 2000076500	A3	20010712		

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

WO 2000064441 A2 20001102 WO 2000-SE819 20000428

WO 2000064441 A3 20010614

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2000058619 A5 20010102 AU 2000-58619 20000615

EP 1185263 A2 20020313 EP 2000-944534 20000615

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

JP 2003501462 T2 20030114 JP 2001-502833 20000615

AU 2001025663 A5 20011224 AU 2001-25663 20001220

AU 2001025664 A5 20011224 AU 2001-25664 20001220

PRIORITY APPLN. INFO.:

SE 1999-2251 A 19990615

SE 1999-2252 A 19990615

US 1999-139632P P 19990617

US 1999-139633P P 19990617

WO 2000-SE819 W 20000428

SE 1999-1531 A 19990428

US 1999-131355P P 19990428

SE 1999-1906 A 19990526

US 1999-136604P P 19990527

WO 2000-SE1267 W 20000615

WO 2000-SE2612 W 20001220

WO 2000-SE2613 W 20001220

AB The present invention relates to a compound having agonist activity to the 5-HT₄ receptor for use as a medicament and to the use of said compds. in the manufacture of a medicament for use in therapeutic or prophylactic treatment of disorders involving bronchocontraction of a human or animal body, as well as methods of treatment, wherein said compds. are administered. The present invention also relates to a compound having antagonist activity to the 5-HT₃ receptor for use as a medicament and to the use of said compound in the manufacture of a medicament for use in therapeutic or prophylactic treatment of disorders involving bronchocontraction of a human or animal body, as well as methods of treatment, wherein said compds. are administered. An example is given showing that the selective 5-HT₄ receptor agonist RS 67333 gives a strong sustained relaxing effect on the spontaneous tone in human in vitro preps.

IC ICM A61K031-4045

ICS A61P011-08; A61P011-06

CC 1-9 (Pharmacology)

ST serotonergic agonist antagonist bronchodilator

IT 5-HT antagonists

(5-HT₃; 5-HT₄ receptor agonists
and 5-HT₃ receptor antagonists for treatment of
bronchocontraction)

IT Antidepressants
Bronchodilators
Psychotropics
(5-HT₄ receptor agonists and 5-
HT₃ receptor antagonists for treatment of bronchocontraction)

IT 5-HT agonists
(5-HT₄; 5-HT₄ receptor agonists
and 5-HT₃ receptor antagonists for treatment of
bronchocontraction)

IT 168986-60-5, RS 67333
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(5-HT₄ receptor agonists and 5-
HT₃ receptor antagonists for treatment of bronchocontraction)

IT 50-53-3, Chlorpromazine, biological studies 50-67-9,
5-Hydroxytryptamine, biological studies 55-45-8 58-38-8,
Prochlorperazine 58-39-9, Perphenazine 69-23-8, Fluphenazine
117-89-5, Trifluoperazine 364-62-5, Metoclopramide 487-93-4,
5-Hydroxy-N,N-dimethyltryptamine 548-73-2, Droperidol 608-07-1,
5-Methoxytryptamine 3546-03-0, Cyamemazine 4774-24-7, Quipazine
5786-21-0, Clozapine 21236-55-5, QX 222 23210-56-2, Ifenprodil
28614-26-8, N-Methylquipazine 39133-31-8, Trimebutine 39478-62-1
40796-97-2, MDL 72222 42399-41-7, Diltiazem 57818-92-5, TMB 8
64097-94-5 66564-14-5, Cinitapride 74885-09-9, 5-Carboxamidotryptamine
75272-39-8, YM-09151 76272-78-1, BRL 24682 78950-78-4,
8-Hydroxy-2-dipropylaminotetralin 81098-60-4, Cisapride 85273-96-7,
ICI 169369 85650-52-8, Mirtazapine 86811-09-8, Litoxetine
89565-68-4, ICS-205930 90182-92-6, Zalcopride 98330-05-3, Anpirtoline
99390-76-8, BRL 20627 99614-02-5, GR 38032 100648-19-9, RU 28253
101626-70-4, Talipexole 106243-16-7, Thioperamide 106469-51-6, CF
109203 109216-58-2, LY 278584 109872-41-5, BRL 24924 109889-09-0,
BRL-43694 112727-80-7, Renzapride 112885-41-3, Mosapride
113140-33-3, GR 65630 115753-79-2, Galanolactone 115956-12-2,
Dolasetron 115956-13-3, Dolasetron mesylate 120635-74-7, Cilansetron
120713-18-0, BMJ 33462 121650-80-4, Pancopride 122732-06-3
122852-42-0, Alosetron 122866-79-9, R076186 123040-69-7, Azasetron
123258-84-4, Itasetron 123441-85-0 123482-22-4, Zatosetron
125557-35-9, ML-1035 127595-11-8, DAU 6236 127595-43-1, BIMU 1
127618-28-4, Dau 6215 128200-30-6, L-683877 129299-90-7, FK 1052
132036-88-5, Ramosetron 134296-40-5, BIMU 8 135729-55-4, RS-42358-197
135729-61-2, Palonosetron 135729-62-3, RS-25259-197 136013-69-9, Way
100289 136174-04-4, RG 12915 138752-34-8, RS 56532 139094-48-7, KF
18259 140865-88-9, BRL 46470A 141034-42-6, DAT-582 141196-99-8, Sc
53116 141533-35-9, SDZ 216-525 142228-17-9, TKS159
143137-35-3, RS-56812 143137-37-5, RS-056812-198 143178-84-1, MDL
72699 143381-68-4, ADR 882 143407-29-8, Iodophenpropit 145082-87-7,
KF 17643 146388-57-0, SC-49518 147600-74-6, SC-52491 148565-09-7,
KB-R 6933 148702-58-3, SB 204070 148868-55-7, ML 10302 149719-06-2,
RS 23597-190 155106-73-3, VB20B7 160599-89-3, VA 21B7 162413-52-7,
GK 128 166743-12-0, SK-951 166815-18-5, RS17017 168986-61-6, RS
67506 172679-55-9, SR59768 179474-80-7, R093877 179474-81-8,
Prucalopride 179913-42-9 189188-57-6, Zelmec 193404-36-3, RS 57639
207605-20-7 220850-98-6, YM-53389 303955-07-9, YM-47813
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(5-HT₄ receptor agonists and 5-
HT₃ receptor antagonists for treatment of bronchocontraction)

IT 123805-17-4, ADR 851
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (ADR 851; 5-HT₄ receptor agonists and 5-HT₃ receptor antagonists for treatment of bronchocontraction)

IT 138559-58-7, ADR 932
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (ADR 932; 5-HT₄ receptor agonists and 5-HT₃ receptor antagonists for treatment of bronchocontraction)

IT 160472-97-9, N 3389
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (N 3389; 5-HT₄ receptor agonists and 5-HT₃ receptor antagonists for treatment of bronchocontraction)

IT 161362-69-2, RS 67532
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (RS 67532; 5-HT₄ receptor agonists and 5-HT₃ receptor antagonists for treatment of bronchocontraction)

IT 175413-81-7, SB 205149
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (SB 205149; 5-HT₄ receptor agonists and 5-HT₃ receptor antagonists for treatment of bronchocontraction)

IT 169789-38-2, SDZ 216-454
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (SDZ 216-454; 5-HT₄ receptor agonists and 5-HT₃ receptor antagonists for treatment of bronchocontraction)

IT 99614-01-4, SN 307
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (SN 307; 5-HT₄ receptor agonists and 5-HT₃ receptor antagonists for treatment of bronchocontraction)

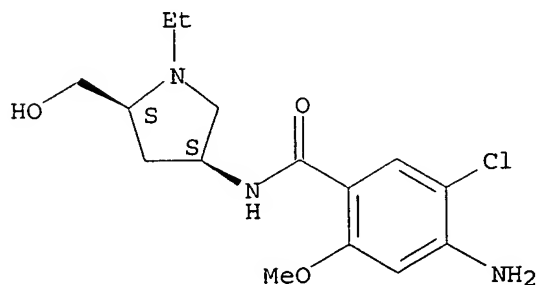
IT 148611-75-0, WAY 100579
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (WAY 100579; 5-HT₄ receptor agonists and 5-HT₃ receptor antagonists for treatment of bronchocontraction)

IT 153608-99-2, YM 114
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (YM 114; 5-HT₄ receptor agonists and 5-HT₃ receptor antagonists for treatment of bronchocontraction)

IT 142228-17-9, TKS159
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (5-HT₄ receptor agonists and 5-HT₃ receptor antagonists for treatment of bronchocontraction)

RN 142228-17-9 CAPLUS
 CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L86 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:772451 CAPLUS

DOCUMENT NUMBER: 133:329581

TITLE:

Serotonergic agonists and antagonists for

treatment of bronchoconstriction

INVENTOR(S): Skogvall, Stefan

PATENT ASSIGNEE(S): Respiratorius AB, Swed.

SOURCE:

PCT Int. Appl., 28 pp.

CODEN: PIXXD2

PATENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2000064441 A2 20001102 WO 2000-SE819 20000428

WO 2000064441 A3 20010614

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN,

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RW: GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1173168 A2 20020123 EP 2000-937417 20000428

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

JP 2002542287 T2 20021210 JP 2000-613432 20000428

WO 2000076500 A2 20001221 WO 2000-SE1267 20000615

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN,

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EP 1185263 A2 20020313 EP 2000-944534 20000615

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

JP 2003501462 T2 20030114 JP 2001-502833 20000615

US 2002173505 A1 20021121

PRIORITY APPLN. INFO.:

JP 2003501462 T2 20030114

US 2002173505 A1 20021121

US 1999-131355P SE 1999-1531

US 1999-136604P SE 1999-1906

US 1999-139633P SE 1999-2252

US 1999-139632P SE 1999-2251

US 1999-139631P SE 1999-2251

US 1999-139630P SE 1999-2251

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US 1999-139465P SE 1999-2251

US 1999-139464P SE 1999-2251

US 1999-139463P SE 1999-2251

US 1999-139462P SE 1999-2251

US 1999-139461P SE 1999-2251

AB The present invention relates to a compound having agonist activity to the 5-HT₄ receptor or antagonist activity to the 5-HT_{2A} receptor and manufacture of a medicament for prophylactic or therapeutic treatment of disorders involving bronchoconstriction of a human or animal, such as asthma, emphysema, chronic bronchitis, chronic obstructive pulmonary disease, depression, anorectic or bulimic eating disorders, anxiety or various psychotic conditions including reducing the pathol. bronchoconstriction by at least 30%, preferably at least 60%, and most preferably at least 90%.

IC ICM A61K031-395

CC 1-7 (Pharmacology)

ST Section cross-reference(s): 63

serotonergic agonist antagonist bronchoconstriction; antiasthmatic serotonergic agonist antagonist; anxiolytic serotonergic agonist antagonist; antipsychotic 5-HT antagonist serotonergic agonist antagonist

IT (5-HT_{2A}; serotonergic agonists and antagonists for treatment of bronchoconstriction-related disorders) 5-HT agonists (5-HT₄; serotonergic agonists and antagonists for treatment of bronchoconstriction-related disorders)

IT Bronchi (bronchoconstriction; serotonergic agonists and antagonists for treatment of bronchoconstriction-related disorders)

IT Appetite (bulimia; serotonergic agonists and antagonists for treatment of bronchoconstriction-related disorders)

IT Bronchi (chronic bronchitis; serotonergic agonists and antagonists for treatment of bronchoconstriction-related disorders)

IT Lung, disease (chronic obstructive; serotonergic agonists and antagonists for treatment of bronchoconstriction-related disorders)

IT Anorexia (anorexia; serotonergic agonists and antagonists for treatment of bronchoconstriction-related disorders)

IT Antiasthmatics Antidepressants Antipsychotics Anxiolytics Bronchodilators Drug delivery systems Emphysema Schizophrenia

IT (serotonergic agonists and antagonists for treatment of bronchoconstriction-related disorders)

50-37-3, LSD 50-49-7, Imipramine 50-67-9D, Serotonin, derivs. 110-85-0D, Piperazine, aryl derivs., biological studies 129-03-3, Cyproheptadine 361-37-5, Methysergide 364-62-5, Metoclopramide 487-93-4, 5-Hydroxy-N,N-dimethyltryptamine 510-74-7, AMI-193 548-43-6, Elymoclavine 608-07-1, 5-Methoxytryptamine 749-02-0, Spiperone 4205-90-7, Clonidine 5560-72-5, Iprindole 15574-96-6, Pizotifen 16357-59-8, N-Ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline 17692-51-2, Metergoline 20980-22-7D, 1-(2-Pyrimidinyl)piperazine, derivs. 24219-97-4, Mianserin 28299-33-4D, Imidazoline, arylalkyl derivs. 32359-34-5, Medifoxamine 32896-53-0, LY 53857 free base 54739-18-3, Fluvoxamine 54910-89-3,

Fluoxetine 59729-33-8, Citalopram 61869-08-7, Paroxetine 64795-35-3,
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 (R,R)-LY-53857 99746-70-0, (S,R)-LY-53857 99746-72-2, (R,S)-LY-53857
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 112192-04-8, Roxindole 112727-80-7, Renzapride 112885-41-3, Mosapride
 112922-55-1, Cericlamine 120444-71-5, Deramciclane 121588-75-8,
 Amesergide 122866-79-9, R 076186 125557-35-9 125926-17-2,
 Sarpogrelate 127266-56-2, WY 50324 127595-11-3, DAU 6236
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 132539-06-1, Olanzapine 133364-63-3, DV 7028 134296-40-5, BIMU 8
 136861-96-6, MDL 28133A 137328-52-0, LY 215840 138752-34-8, RS 56532
 139290-65-6, MDL 100907 139290-69-0, MDL 100151 141196-99-8, SC-53116
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 150527-23-4 150527-36-9, FG5893 hydrochloride 153415-44-2
 155106-73-3, VB 20B7 161178-10-5, YM 992 161362-69-2, RS 67532
 166743-12-0, SK-951 166815-18-5, RS 17017 167933-07-5, BIMT 17
 168986-60-5, RS 67333 168986-61-6, RS 67506 169789-38-2, SDZ 216-454
 172679-55-9, SR59768 175413-81-7, SB 205149 178485-02-4, ALEPH-2
 179474-80-7, R 093877 179474-81-8, Prucalopride 183949-64-6, NRA0045
 189188-57-6, Zelmec 193404-36-3, RS 57639 208661-17-0, LU 111995
 217635-62-6 217635-64-8 220850-98-6, YM 53389 303953-05-1
 303953-06-2 303955-07-9, YM 47813

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(serotonergic agonists and antagonists for treatment of bronchoconstriction-related disorders)

IT 142228-17-9, TKS 159

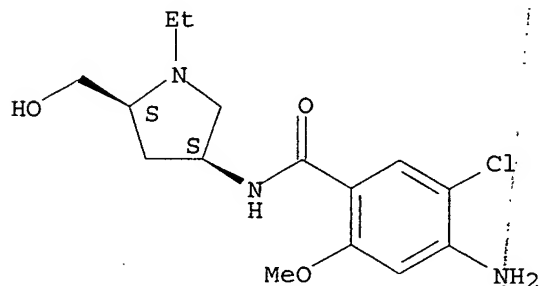
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(serotonergic agonists and antagonists for treatment of bronchoconstriction-related disorders)

RN 142228-17-9 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:722082 CAPLUS

DOCUMENT NUMBER: 129:337877

TITLE: New *gastroprokinetic* agent TKS159:
4-amino-5-chloro-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]-2-methoxybenzamideAUTHOR(S): Adachi, Tsutomu; Mizoguchi, Jun-Ichi; Hayashi, Yasuo;
Yamashoji, Yuko; Kanehisa, Nobuko; Kai, Yasushi;
Inoue, YoshihisaCORPORATE SOURCE: Res. and Dev. Dep., Teikoku Chem. Industries Co. Ltd,
Hyogo, 664, JapanSOURCE: Acta Crystallographica, Section C: Crystal Structure
Communications (1998), C54(10), 1527-1529
CODEN: ACSCEE; ISSN: 0108-2701

PUBLISHER: Munksgaard International Publishers Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The absolute configuration of the title compound (TKS159, C15H22ClN3O3) was determined. Crystallog. data are given. The bent conformation of the mol., in which the aromatic and pyrrolidine rings are at nearly 60° to each other, is maintained by intra- and intermol. H bonds. A three-dimensional network of H bonds is formed among the amino, hydroxy and carbonyl groups of neighboring mols.

CC 75-8 (Crystallography and Liquid Crystals)

Section cross-reference(s): 6, 27, 63

ST mol structure amino ethylhydroxymethylpyrrolidinyl methoxy benzamide;
structure amino chloro ethylhydroxymethylpyrrolidinyl methoxy benzamide;
gastroprokinetic agent TKS159 abs conformation structure

IT 142228-17-9, TKS159

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)

(crystal structure and absolute configuration of)

IT 142228-17-9, TKS159

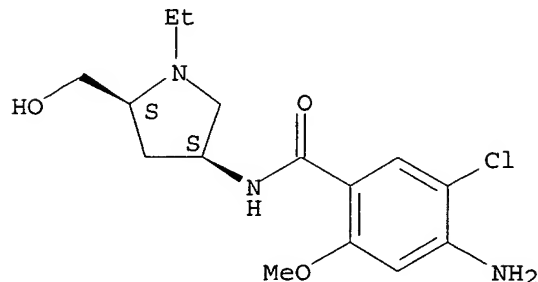
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)

(crystal structure and absolute configuration of)

RN 142228-17-9 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

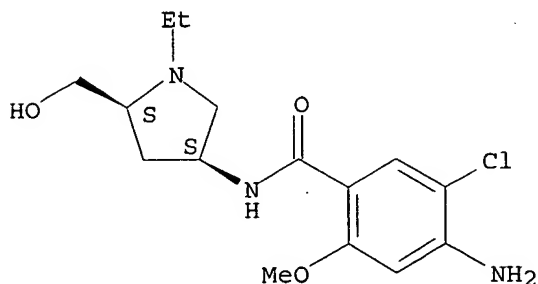
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:630754 CAPLUS
 DOCUMENT NUMBER: 127:298740
 TITLE: Pharmaceutical compositions
 INVENTOR(S): Shii, Noritoshi; Shinoda, Masamitsu; Watanabe, Hajime;
 Yonetani, Akimasa
 PATENT ASSIGNEE(S): Teikoku Hormone Mfg. Co., Ltd., Japan; Takada Seiyaku
 K. K.
 SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	JP 09249561	A2	19970922	JP 1996-100693	19960315
PRIORITY APPLN. INFO.:				JP 1996-100693	19960315
AB	Pharmaceutical comps. [e.g. tablets] contain 4-amino-5-chloro-2-methoxy-N-[(2S, 4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidiny]benzamide with addition of sugar alcs., starch, monosaccharides, sucrose, stearic acid or its salts and/or talc to improve stability and bioavailability.				
IC	ICM A61K031-40 ICS A61K047-04; A61K047-10; A61K047-12; A61K047-26; A61K047-36; C07D207-08; C07M007-00				
CC	63-6 (Pharmaceuticals)				
IT	57-11-4, Stearic acid, biological studies 57-50-1, Sucrose, biological studies 69-65-8, Mannitol 557-04-0, Magnesium stearate 1592-23-0, Calcium stearate 9004-32-4, CM-cellulose Na salt 9005-25-8, Starch, biological studies 9005-25-8D, Starch, alphasized, biological studies 9049-76-7, HydroxypropylStarch 14807-96-6, Talc, biological studies 142228-17-9 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical comps.)				
IT	142228-17-9 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical comps.)				
RN	142228-17-9 CAPLUS				
CN	Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidiny]-2-methoxy- (9CI) (CA INDEX NAME)				

Absolute stereochemistry.



L86 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1998:20177 CAPLUS

DOCUMENT NUMBER: 128:162589
 TITLE: Novel phenyl nitrogen mustard and half-mustard derivatives of distamycin A
 AUTHOR(S): Cozzi, Paolo; Beria, Italo; Biasoli, Giovanni; Caldarelli, Marina; Capolongo, Laura; D'alessio, Roberto; Geroni, Cristina; Mazzini, Stefania; Ragg, Enzo; Rossi, Carla; Mongelli, Nicola
 CORPORATE SOURCE: Pharmacia and Upjohn, Therapeutic Area Oncology and Immunology, Preclinical Research, Milan, 20014, Italy
 SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(23), 2985-2990
 CODEN: BMCLE8; ISSN: 0960-894X
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The design, synthesis, in vitro and in vivo activities of novel benzoyl and cinnamoyl nitrogen mustard and half-mustard derivs. of distamycin A are described and structure-activity relationships are discussed. The equipotent activities of N-ethyl-N-chloroethyl half-mustards and N,N-dichloroethyl mustards and the superior activities of cinnamoyl derivs. are the most relevant features of the series.

CC 1-6 (Pharmacology)

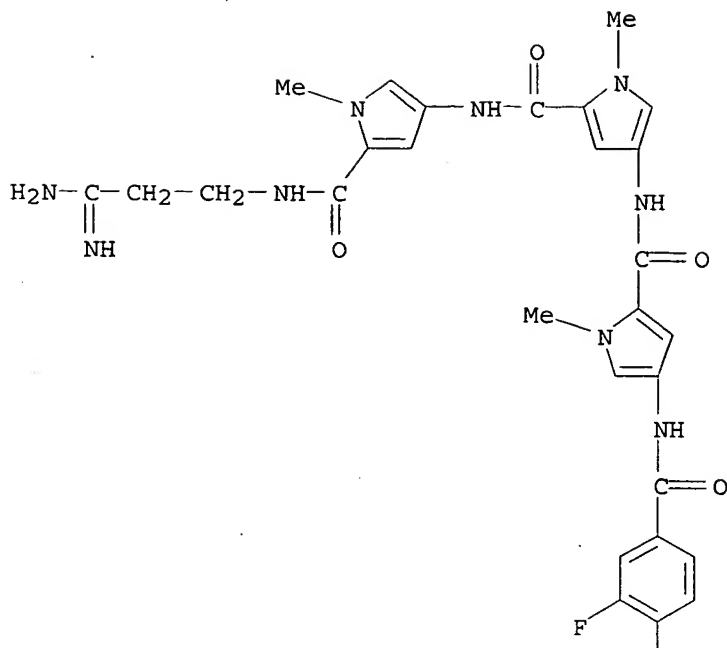
IT 118438-45-2 187802-29-5 187802-31-9 194482-64-9 194482-65-0
 194482-84-3 203114-22-1 203118-05-2 203118-08-5 203118-13-2
 203118-15-4 203118-21-2 203118-22-3 203118-29-0
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (preparation and antitumor activity of Ph nitrogen mustard and half-mustard derivs. of distamycin A)

IT 203118-15-4
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (preparation and antitumor activity of Ph nitrogen mustard and half-mustard derivs. of distamycin A)

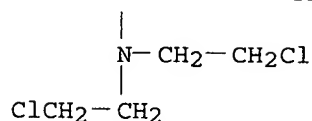
RN 203118-15-4 CAPLUS

CN 1H-Pyrrole-2-carboxamide, N-[5-[[[3-amino-3-iminopropyl)amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-4-[[[4-[[4-[bis(2-chloroethyl)amino]-3-fluorobenzoyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



● HCl

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:586 CAPLUS

DOCUMENT NUMBER: 120:586

TITLE: Benzamide derivative for improvement of *digestive tract* movement

INVENTOR(S): Sakyama, Hideyo; Sekida, Mariko; Shinoda, Masamitsu; Fujiwara, Hiromichi

PATENT ASSIGNEE(S): Teikoku Hormone Mfg Co Ltd, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

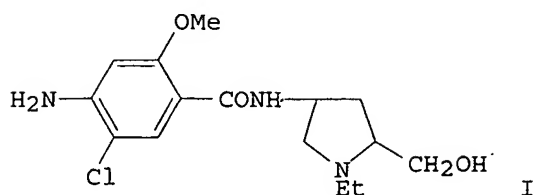
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

in IDS

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05229942	A2	19930907	JP 1992-88444	19920225
JP 3242975	B2	20011225		
PRIORITY APPLN. INFO.:			JP 1992-88444	19920225
GI				



AB Improvers for *digestive tract* movement contain benzamide derivative I or its salts as active ingredients. I does not affect the central nervous system, thus causing no extrapyramidal syndrome, etc. Treatment of 28.0 g 4-amino-5-chloro-2-methoxybenzoic acid with 20 g (2S,4S)-4-amino-N-ethyl-2-hydroxymethylpyrrolidine, 1-hydroxy-1H-benzotriazole, and DCC in CHCl₃ for 14 h gave 26.3 g (2S,4S)-I, which enhanced *digestive tract* movement in mice and showed antiemetic activity in dogs. Film-coated tablets containing (2S,4S)-I were formulated.

IC ICM A61K031-40
ICS C07D207-14

CC 1-9 (Pharmacology)
Section cross-reference(s): 27, 63

ST benzamide improver *digestive tract* movement;
antiemetic benzamide prepn

IT *Digestive tract*
(movement of, improvement of, benzamide derivative for)

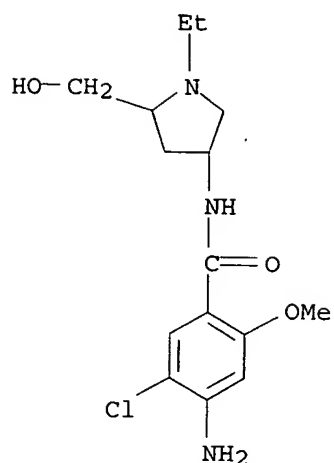
IT 142228-16-8
RL: BIOL (Biological study)
(*digestive tract* movement improvement by)

IT 142228-17-9P 142347-77-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as *digestive tract* movement improver
and antiemetic agent)

IT 142228-16-8
RL: BIOL (Biological study)
(*digestive tract* movement improvement by)

RN 142228-16-8 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)



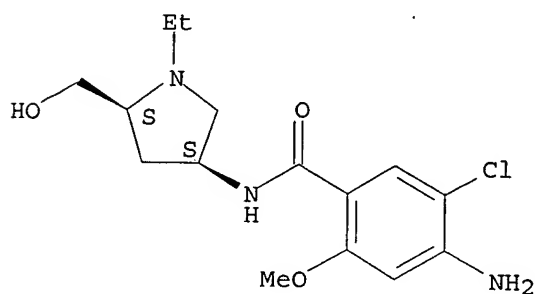
IT 142228-17-9P 142347-77-1P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as *digestive tract* movement improver
and antiemetic agent)

RN 142228-17-9 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

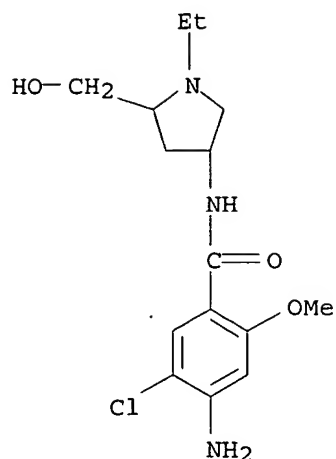
Absolute stereochemistry.



RN 142347-77-1 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride, (3S-cis)- (9CI) (CA INDEX NAME)

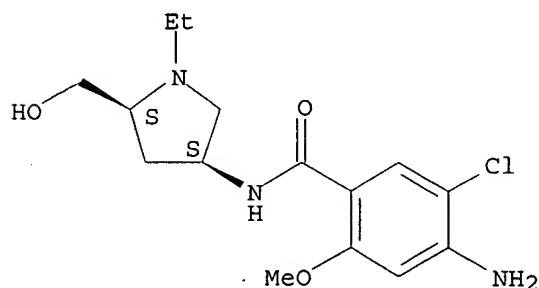
Absolute stereochemistry.



RN 142228-17-9 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

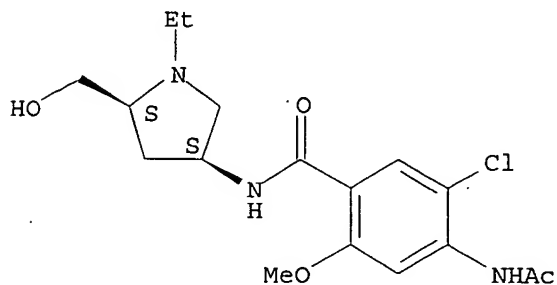
Absolute stereochemistry.



RN 142228-18-0 CAPLUS

CN Benzamide, 4-(acetylamino)-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, (3S-cis)- (9CI) (CA INDEX NAME)

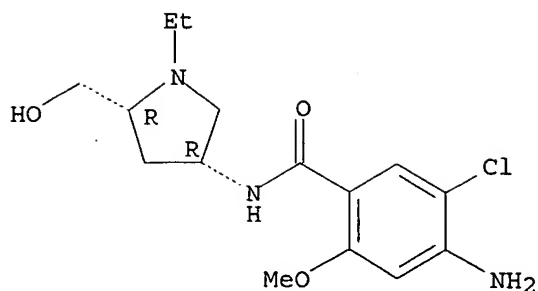
Absolute stereochemistry.



RN 142228-19-1 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[(3R,5R)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

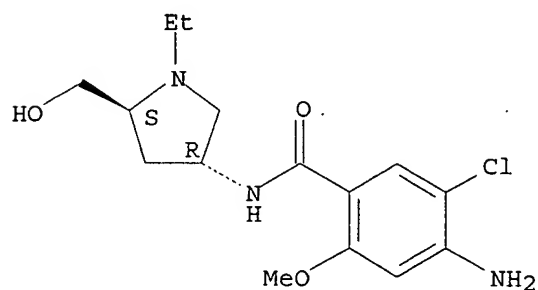
Absolute stereochemistry.



RN 142228-20-4 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[(3R,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

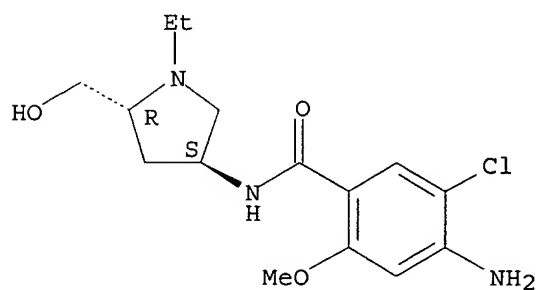
Absolute stereochemistry.



RN 142228-21-5 CAPLUS

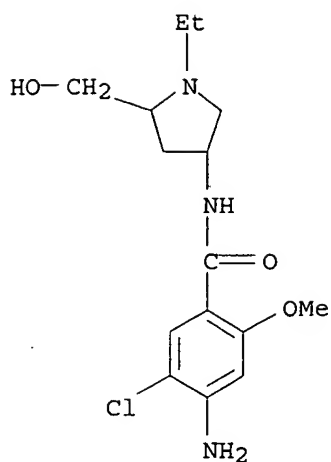
CN Benzamide, 4-amino-5-chloro-N-[(3S,5R)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 142347-67-9 CAPLUS

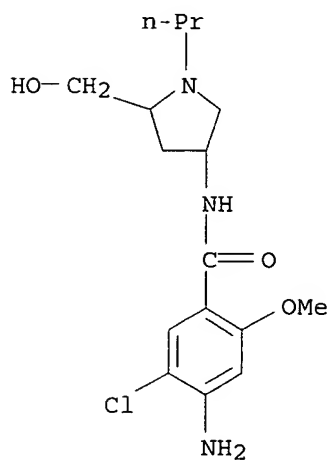
CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 142347-68-0 CAPLUS

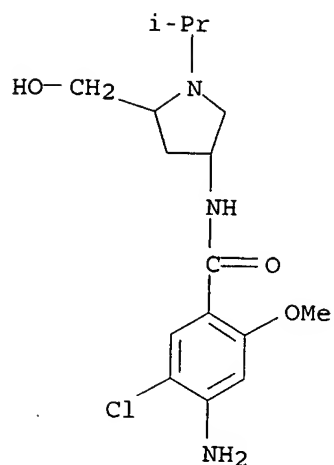
CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-propyl-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

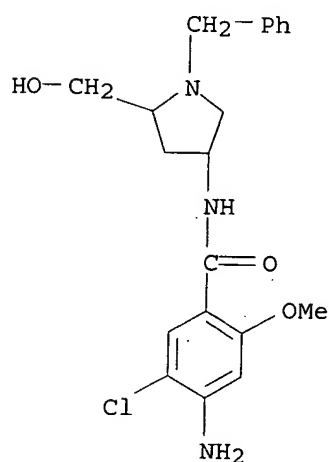
RN 142347-69-1 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-(1-methylethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



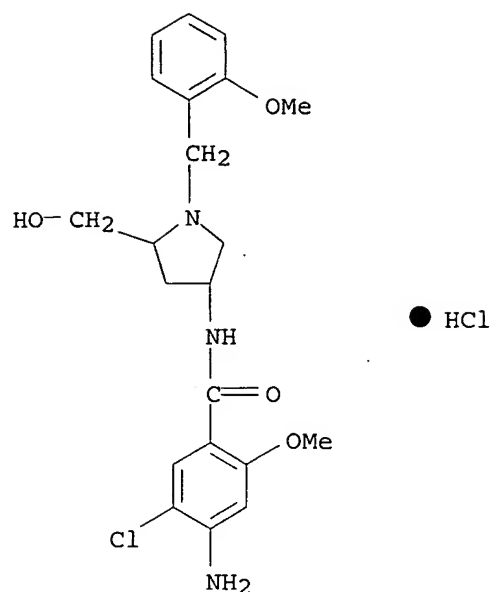
● HCl

RN 142347-70-4 CAPLUS
 CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-(phenylmethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



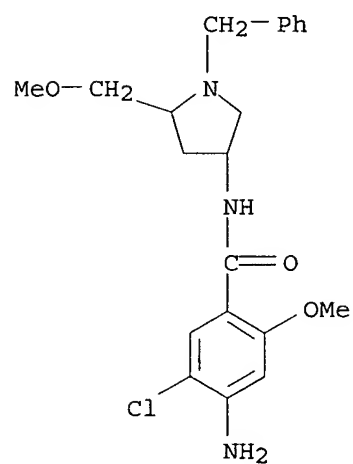
● HCl

RN 142347-71-5 CAPLUS
 CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-[(2-methoxyphenyl)methyl]-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



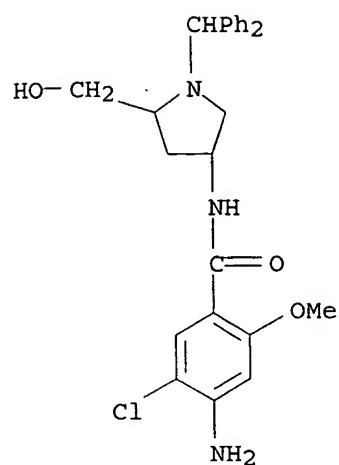
RN 142347-72-6 CAPLUS

CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[5-(methoxymethyl)-1-(phenylmethyl)-3-pyrrolidinyl]-, monohydrochloride (9CI) (CA INDEX NAME)



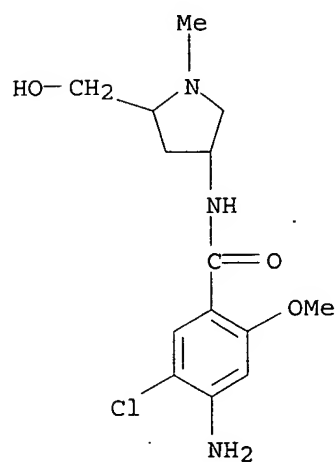
RN 142347-73-7 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[1-(diphenylmethyl)-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



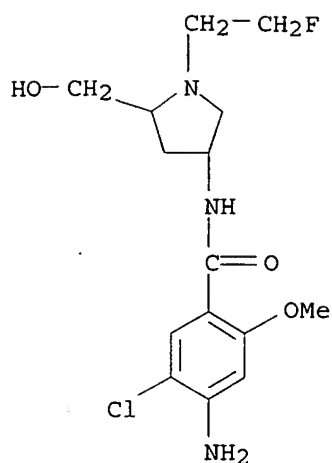
● HCl

RN 142347-74-8 CAPLUS
 CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-methyl-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

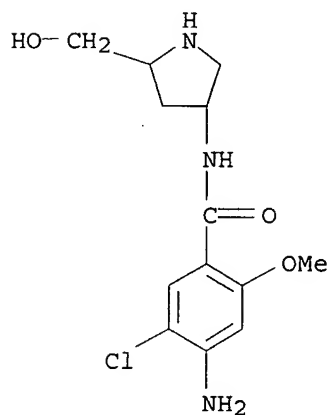
RN 142347-75-9 CAPLUS
 CN Benzamide, 4-amino-5-chloro-N-[1-(2-fluoroethyl)-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 142347-76-0 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)

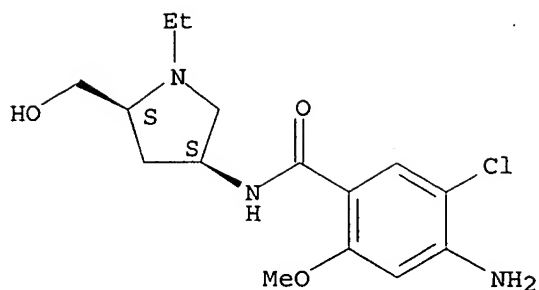


● HCl

RN 142347-77-1 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride, (3S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

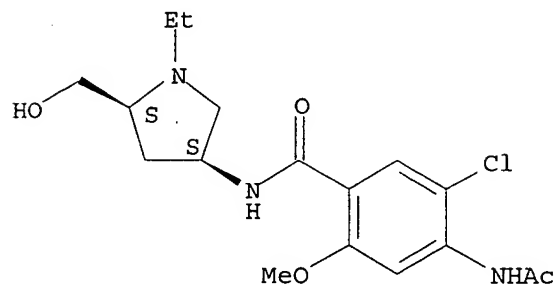


● HCl

RN 142347-78-2 CAPLUS

CN Benzamide, 4-(acetylamino)-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride, (3S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

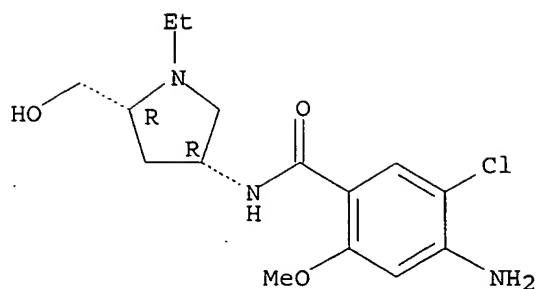


● HCl

RN 142347-79-3 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride, (3R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

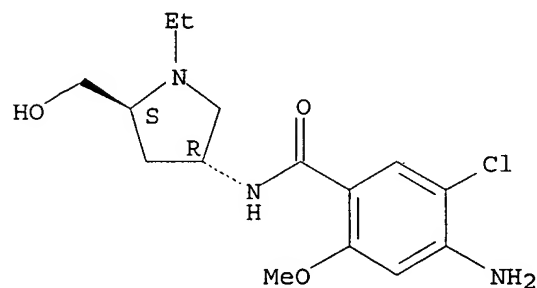


● HCl

RN 142347-80-6 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyll-2-methoxy-, monohydrochloride, (3R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L86 ANSWER 16 OF 22 MEDLINE on STN DUPLICATE 2
 ACCESSION NUMBER: 1998362430 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 9697104
 TITLE: Effect of **TKS159**, a novel 5-hydroxytryptamine₄ agonist, on **gastric** contractile activity in conscious dogs.
 AUTHOR: Haga N; Suzuki H; Shiba Y; Mochiki E; Mizumoto A; Itoh Z
 CORPORATE SOURCE: Gastrointestinal Research Laboratory, Institute for Molecular and Cellular Regulation, Gunma University, Maebashi, Japan.
 SOURCE: Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society, (1998 Aug) Vol. 10, No. 4, pp. 295-303.
 Journal code: 9432572. ISSN: 1350-1925.
 PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199810
 ENTRY DATE: Entered STN: 6 Jan 1999
 Last Updated on STN: 6 Jan 1999
 Entered Medline: 30 Oct 1998

ABSTRACT:

A novel 5-hydroxytryptamine (5-HT)₄ receptor agonist, ***TKS159***, 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl] benzamide, has recently been developed as a ***gastroprokinetic*** drug. Cisapride is already used clinically to increase gastric contractions. The stimulatory effects of ***TKS159*** and cisapride on gastric contractions were examined using force transducers chronically implanted on the vagally denervated pouch (Heidenhain pouch) and the vagally innervated main stomach in conscious dogs. Contractile activity was analysed by computer and expressed as a motor index. Intravenous administration of TKS159 or cisapride significantly increased the motor index in both the main stomach and the Heidenhain pouch during the fed and fasted states. Pharmacological characterization in the fasted state revealed that the contraction-stimulating activity of TKS159 and cisapride on the stomach was significantly inhibited by atropine, hexamethonium and a 5-HT₄ receptor antagonist, SDZ 205-557. Granisetron (a 5-HT₃ receptor antagonist) significantly inhibited cisapride-induced, but not TKS159-induced gastric contractions. The plasma ***motilin*** concentration was significantly increased after cisapride, but not after TKS159 injection. In conclusion, TKS159 has a contractile-stimulating effect on both the innervated and the denervated stomach. It is likely that a cholinergic pathway and 5-HT₄ receptors are involved in producing the contractions, although other mechanisms cannot be excluded. Cisapride has almost the same characteristics, but the present findings suggest the involvement of ***motilin*** and 5-HT₃ receptors in the effects of cisapride.

CONTROLLED TERM: Animals
 *Cisapride: PD, pharmacology
 Dogs
 Drug Evaluation, Preclinical
 *Gastrointestinal Agents: PD, pharmacology
 Gastrointestinal Motility: DE, drug effects
 Motilin: AN, analysis
 Muscle Contraction: DE, drug effects
 *Pyrrolidines: PD, pharmacology
 *Serotonin Agonists: PD, pharmacology
 Stimulation, Chemical
 *Stomach: DE, drug effects
 Stomach: IR, innervation
 Transducers
 Vagus Nerve: DE, drug effects
 CAS REGISTRY NO.: 52906-92-0 (Motilin); 81098-60-4 (Cisapride)
 CHEMICAL NAME: 0 (Gastrointestinal Agents); 0 (Pyrrolidines); 0 (Serotonin Agonists); 0 (TKS159)

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ACCESSION NUMBER: 2003052515 EMBASE
 TITLE: 5-HT₄ receptor ligands: Applications and new prospects.

AUTHOR: Langlois M.; Fischmeister R.
 CORPORATE SOURCE: M. Langlois, CNRS-BIOCIS (UPRES A 8076), Faculte de Pharmacie, F-92296 Chatenay-Malabry Cedex, France. zacopride@aol.com
 SOURCE: Journal of Medicinal Chemistry, (30 Jan 2003) Vol. 46, No. 3, pp. 319-344. .
 Refs: 261
 ISSN: 0022-2623 CODEN: JMCMAR
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
 030 Pharmacology;
 037 Drug Literature Index
 038 Adverse Reactions Titles
 048 Gastroenterology
 LANGUAGE: English
 ENTRY DATE: Entered STN: 20 Feb 2004
 Last Updated on STN: 20 Feb 2004
 CONTROLLED TERM: Medical Descriptors:
 *drug mechanism
 drug effect
 drug activity
 drug structure
 structure activity relation
 drug potency
 drug determination
 drug synthesis
 stomach motility
 drug receptor binding
 receptor affinity
 stereochemistry
 drug selectivity
 drug bioavailability
 pharmacophore
 binding site
 protein localization
 cardiovascular system
 heart arrhythmia: SI, side effect
 tachycardia: SI, side effect
 long QT syndrome: SI, side effect
 torsade des pointes: SI, side effect
 Herxheimer reaction: SI, side effect
 behavior
 cognition
 memory
 Alzheimer disease
 adrenal gland
 human
 nonhuman
 review
 CONTROLLED TERM: Drug Descriptors:
 *serotonin 4 antagonist: AN, drug analysis
 *serotonin 4 antagonist: CM, drug comparison
 *serotonin 4 antagonist: DV, drug development
 *serotonin 4 antagonist: PK, pharmacokinetics
 *serotonin 4 antagonist: PD, pharmacology
 *serotonin 4 antagonist: PO, oral drug
 administration
 *serotonin 4 agonist: AE, adverse drug reaction
 *serotonin 4 agonist: AN, drug analysis

*serotonin 4 agonist: CM, drug comparison
 *serotonin 4 agonist: DV, drug development
 *serotonin 4 agonist: DO, drug dose
 *serotonin 4 agonist: PK, pharmacokinetics
 *serotonin 4 agonist: PD, pharmacology
 *serotonin 4 agonist: PO, oral drug administration
 *serotonin 4 receptor: EC, endogenous compound
 metoclopramide: AE, adverse drug reaction
 metoclopramide: AN, drug analysis
 metoclopramide: CM, drug comparison
 metoclopramide: PD, pharmacology
 bemisetron: AN, drug analysis
 bemisetron: CM, drug comparison
 bemisetron: PD, pharmacology
 tropisetron: AN, drug analysis
 tropisetron: CM, drug comparison
 tropisetron: PD, pharmacology
 renzapride: AE, adverse drug reaction
 renzapride: AN, drug analysis
 renzapride: CM, drug comparison
 renzapride: PD, pharmacology
 zacopride: AN, drug analysis
 zacopride: CM, drug comparison
 zacopride: PD, pharmacology
 cisapride: AE, adverse drug reaction
 cisapride: AN, drug analysis
 cisapride: PD, pharmacology
 ondansetron: AN, drug analysis
 ondansetron: CM, drug comparison
 ondansetron: PD, pharmacology
 3 ethyl 2,3 dihydro 2 oxo 1 benzimidazolecarboxylic acid
 3alpha tropanylamide: AN, drug analysis
 3 ethyl 2,3 dihydro 2 oxo 1 benzimidazolecarboxylic acid
 3alpha tropanylamide: PD, pharmacology
 2,3 dihydro 3 isopropyl 2 oxo 1 benzimidazolecarboxylic
 acid 3alpha tropanylamide: AN, drug analysis
 2,3 dihydro 3 isopropyl 2 oxo 1 benzimidazolecarboxylic
 acid 3alpha tropanylamide: PD, pharmacology
 itasetron: AN, drug analysis
 itasetron: PD, pharmacology
 8 amino 7 chloro 1,4 benzodioxan 5 carboxylic acid 1 butyl
 4 piperidinylmethyl ester: AN, drug analysis
 8 amino 7 chloro 1,4 benzodioxan 5 carboxylic acid 1 butyl
 4 piperidinylmethyl ester: DV, drug development
 8 amino 7 chloro 1,4 benzodioxan 5 carboxylic acid 1 butyl
 4 piperidinylmethyl ester: DO, drug dose
 8 amino 7 chloro 1,4 benzodioxan 5 carboxylic acid 1 butyl
 4 piperidinylmethyl ester: PD, pharmacology
 8 amino 7 chloro 1,4 benzodioxan 5 carboxylic acid 1 butyl
 4 piperidinylmethyl ester: PO, oral drug administration
 clebopride: AN, drug analysis
 clebopride: PD, pharmacology
 1 (4 amino 5 chloro 2 methoxyphenyl) 3 (1 butyl 4
 piperidinyl) 1 propanone: AN, drug analysis
 1 (4 amino 5 chloro 2 methoxyphenyl) 3 (1 butyl 4
 piperidinyl) 1 propanone: DV, drug development
 1 (4 amino 5 chloro 2 methoxyphenyl) 3 (1 butyl 4
 piperidinyl) 1 propanone: PK, pharmacokinetics
 1 (4 amino 5 chloro 2 methoxyphenyl) 3 (1 butyl 4
 piperidinyl) 1 propanone: PD, pharmacology

4 amino 5 chloro n (octahydro 6 methyl 2h quinolizin 2 yl)
 ortho anisamide: AN, drug analysis
 4 amino 5 chloro n (octahydro 6 methyl 2h quinolizin 2 yl)
 ortho anisamide: PD, pharmacology
 1 methyl 3 indolecarboxylic acid [1 [2
 (methylsulfonylamino)ethyl] 4 piperidinylmethyl] ester: AN,
 drug analysis
 1 methyl 3 indolecarboxylic acid [1 [2
 (methylsulfonylamino)ethyl] 4 piperidinylmethyl] ester: DV,
 drug development
 1 methyl 3 indolecarboxylic acid [1 [2
 (methylsulfonylamino)ethyl] 4 piperidinylmethyl] ester: PK,
 pharmacokinetics
 1 methyl 3 indolecarboxylic acid [1 [2
 (methylsulfonylamino)ethyl] 4 piperidinylmethyl] ester: PD,
 pharmacology
 serotonin 3 antagonist: AN, drug analysis
 serotonin 3 antagonist: CM, drug comparison
 serotonin 3 antagonist: PD, pharmacology
 4 amino 5 chloro n [(hexahydro 1h pyrrolizin 1 yl)methyl] 2
 methoxybenzamide: AN, drug analysis
 4 amino 5 chloro n [(hexahydro 1h pyrrolizin 1 yl)methyl] 2
 methoxybenzamide: CM, drug comparison
 4 amino 5 chloro n [(hexahydro 1h pyrrolizin 1 yl)methyl] 2
 methoxybenzamide: DV, drug development
 4 amino 5 chloro n [(hexahydro 1h pyrrolizin 1 yl)methyl] 2
 methoxybenzamide: PD, pharmacology
 tegaserod: AN, drug analysis
 tegaserod: PD, pharmacology
 piboserod: AN, drug analysis
 piboserod: DV, drug development
 piboserod: PD, pharmacology
 piboserod: PO, oral drug administration
 4 amino 5 chloro 2,3 dihydro 2 methyl n [2 (8
 pyrrolizidinyl)ethyl]benzo[b]furan 7 carboxamide: AN, drug
 analysis
 4 amino 5 chloro 2,3 dihydro 2 methyl n [2 (8
 pyrrolizidinyl)ethyl]benzo[b]furan 7 carboxamide: CM, drug
 comparison
 4 amino 5 chloro 2,3 dihydro 2 methyl n [2 (8
 pyrrolizidinyl)ethyl]benzo[b]furan 7 carboxamide: PD,
 pharmacology
 1 (4 amino 5 chloro 2 methoxyphenyl) 3 [1 [2
 (methanesulfonamido)ethyl] 4 piperidinyl] 1 propanone: AN,
 drug analysis
 1 (4 amino 5 chloro 2 methoxyphenyl) 3 [1 [2
 (methanesulfonamido)ethyl] 4 piperidinyl] 1 propanone: PD,
 pharmacology
 prucalopride: AN, drug analysis
 prucalopride: PD, pharmacology
 mosapride citrate: AN, drug analysis
 mosapride citrate: PD, pharmacology
 4 amino 5 chloro 2 methoxybenzoic acid 3 piperidinopropyl
 ester: AN, drug analysis
 4 amino 5 chloro 2 methoxybenzoic acid 3 piperidinopropyl
 ester: PD, pharmacology
 4 amino 5 chloro 2 methoxybenzoic acid 2
 (diethylamino)ethyl ester: AN, drug analysis
 4 amino 5 chloro 2 methoxybenzoic acid 2
 (diethylamino)ethyl ester: PD, pharmacology

benzoic acid derivative: AN, drug analysis
benzoic acid derivative: PD, pharmacology
unindexed drug
sb 207058
ts 951 k
ml 1035
brl 24682
sc 52246
6 chloro n [(hexahydro 1h pyrrolizin 1
yl)methyl]imidazo[1,2 a]pyridine 8 carboxamide
4 amino 5 chloro n [2 (1 dimethylamino 1 cyclohexyl)ethyl]
2 methoxybenzamide
sc 52491
y 34959
4 amino 5 chloro 2 methoxybenzoic acid 2 (1
piperidinyl)ethyl ester
4 amino 5 chloro 2 methoxybenzoic acid 2 (3,5
dimethylpiperidino)ethyl ester
2 chloro 5 methoxy 4 [5 (2 piperidylmethyl) 1,2,4 oxadiazol
3 yl]aniline
sb 205800
8 amino 7 iodo 1,4 benzodioxan 5 carboxylic acid 1 butyl 4
piperidinylmethyl ester
rs 17017
rs 67532
rs 39604
rs 100302
rs 100235
3 indolecarboxylic acid 2 (1 piperidinyl)ethyl ester
gr 124487
sb 204139
n [2 [4 (1 adamantanecarboxamido) 1 piperidinyl]ethyl] 1
isopropyl 1h indazole 3 carboxamide
2,3 dihydro 2 oxo 1 benzimidazolecarboxylic acid 6 methoxy
3alpha tropanyl ester
ts 951
4 amino 5 chloro n (1 ethyl 2 hydroxymethyl 4 pyrrolidinyl)
2 methoxybenzamide
5 fluoro 2 methoxy 1h indole 3 carboxylic acid 1 [2
(methylsulfonamido)ethyl] 4 piperidinylmethyl ester
(metoclopramide) 12707-59-4; 2576-84-3; 364-62-5;
7232-21-5; (bemesetron) 40796-97-2; (tropisetron)
89565-68-4; (renzapride) 109872-41-5; (zacopride)
90182-92-6; 99617-34-2; (cisapride) 81098-60-4;
(ondansetron) 103639-04-9; 116002-70-1; 99614-01-4; (3
ethyl 2,3 dihydro 2 oxo 1 benzimidazolecarboxylic acid
3alpha tropanylamide) 127595-43-1; (2,3 dihydro 3 isopropyl
2 oxo 1 benzimidazolecarboxylic acid 3alpha tropanylamide)
134296-40-5; (itasetron) 127618-28-4; (8 amino 7 chloro 1,4
benzodioxan 5 carboxylic acid 1 butyl 4 piperidinylmethyl
ester) 148702-58-3; (clebopride) 55905-53-8; (1 (4 amino 5
chloro 2 methoxyphenyl) 3 (1 butyl 4 piperidinyl) 1
propanone) 168986-60-5; (4 amino 5 chloro n (octahydro 6
methyl 2h quinolizin 2 yl) ortho anisamide) 99390-76-8; (1
methyl 3 indolecarboxylic acid [1 [2
(methylsulfonylamino)ethyl] 4 piperidinylmethyl] ester)
144625-51-4; (4 amino 5 chloro n [(hexahydro 1h pyrrolizin
1 yl)methyl] 2 methoxybenzamide) 141196-99-8; (tegaserod)
145158-71-0; 189188-57-6; (piboserod) 152811-62-6;
178273-87-5; (4 amino 5 chloro 2,3 dihydro 2 methyl n [2 (8

CAS REGISTRY NO.:

pyrrolizidinyl)ethyl]benzo[b]furan-7-carboxamide)-
 166743-12-0; (1 (4-amino-5-chloro-2-methoxyphenyl) 3 [1 (2
 (methanesulfonamido)ethyl] 4 piperidinyl] 1 propanone)
 168986-61-6; (prucalopride) 179474-80-7, 179474-81-8,
 179474-84-1; (mosapride citrate) 112885-42-4; (4-amino-5
 chloro-2-methoxybenzoic acid 3 piperidinopropyl ester)
 149719-06-2; (8-amino-7-iodo-1,4-benzodioxan-5-carboxylic
 acid 1-butyl 4-piperidinylmethyl ester) 148703-08-6; (3
 indolecarboxylic acid 2 (1-piperidinyl)ethyl ester)
 135938-17-9; (2,3-dihydro-2-oxo-1-benzimidazolecarboxylic
 acid 6-methoxy-3 α -tropanyl ester) 123258-98-0; (5
 fluoro-2-methoxy-1H-indole-3-carboxylic acid 1 [2
 (methylsulfonamido)ethyl] 4-piperidinylmethyl ester)
 144625-67-2

CHEMICAL NAME: (1) Sb 204070; (2) Sb 207058; (3) Sb 207266; Ym 53389; Sb
 205800; Sb 207710; Rs 17017; Gr 113808; Rs 67333; Rs 67506;
 Rs 67532; Rs 39604; Rs 100302; Sb 203186; Rs 100235; Gr
 124487; Sb 204139; Ly 353433; Sdz htf 919; Dau 6285; Ts
 951; **Tks 159**; Gr 125487d; Rs 23597 190; Ml 10375;
 Mdl 72222; Ics 205930; Brl 24924; Bimu 1; Bimu 8; Dau 6215;
 Ts 951 k; Ml 1035; Brl 20627; Brl 24682; Sc 53116; Sc
 52246; Sc 53606; Sk 951; Ym 47813; Sc 52491; Y 34959; Sdz
 205557; Ml 10302; Rs 23597

COMPANY NAME: (3) SmithKline Beecham

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ACCESSION NUMBER: 1999377316 EMBASE
 TITLE: **Gastroduodenal motility.**
 AUTHOR: Quigley E.M.M.
 CORPORATE SOURCE: Dr. E.M.M. Quigley, Department of Medicine, Clinical
 Sciences Building, Cork University Hospital, Cork, Ireland.
 equigley@ucc.ie
 SOURCE: Current Opinion in Gastroenterology, (1999) Vol. 15, No. 6,
 pp. 481-491.
 Refs: 172
 ISSN: 0267-1379 CODEN: COGAEK
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 006 Internal Medicine
 037 Drug Literature Index
 048 Gastroenterology
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 18 Nov 1999
 Last Updated on STN: 18 Nov 1999

ABSTRACT: Several major themes emerged over the past year in the area of
 gastroduodenal **motility**. Mostly, these themes represented
 extensions of research areas discussed in prior reviews in this series rather
 than the emergence of completely new concepts. Thus, for example, considerable
 emphasis has again been placed on regional **gastric** motor function in
 dyspepsia and on the role of fundic relaxation and accommodation, in
 particular. Not surprisingly, basic physiologic research has also shown a keen
 interest in the regulation of fundic relaxation. One new and exciting
 development is the recognition of the **stomach's** role in satiety. The
 spectrum of **gastric** motor dysfunction in diabetes mellitus continues
 to be explored, and the important role of hyperglycemia in regulating
 gastric function has been further emphasized. More data have been
 provided on noninvasive alternatives to **gastric** motor function
 testing, and several studies have looked at factors that may influence

variability in these various tests. There have been few innovations over the past year in the therapeutic arena; rather, the indications and limitations of current therapies have been further developed.

CONTROLLED TERM: Medical Descriptors:
 **gastrointestinal motility*
 dyspepsia: DI, diagnosis
 dyspepsia: DT, drug therapy
 satiety
 hyperglycemia: DI, diagnosis
 stomach motility
 stomach paresis: DI, diagnosis
 stomach paresis: ET, etiology
 percutaneous endoscopic gastrostomy
 acupuncture
 human
 article
 Drug Descriptors:
 *histamine h2 receptor antagonist: DT, drug therapy
 *histamine h2 receptor antagonist: PD, pharmacology
 *domperidone: DT, drug therapy
 *domperidone: PD, pharmacology
 *serotonin 4 agonist: DV, drug development
 *serotonin 4 agonist: PD, pharmacology
 *tk5 159: DV, drug development
 *tk5 159: PD, pharmacology
 glucagon like peptide 1: EC, endogenous compound
 erythromycin: DT, drug therapy
 erythromycin: PD, pharmacology
 CAS REGISTRY NO.: (domperidone) 57808-66-9; (glucagon like peptide 1)
 89750-14-1; (erythromycin) 114-07-8, 70536-18-4
 CHEMICAL NAME: *Tks 159*

L86 ANSWER 19 OF 22 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on
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ACCESSION NUMBER: 1995:247381 BIOSIS
 DOCUMENT NUMBER: PREV199598261681
 TITLE: Effect of *TKS159*, a novel 5-hydroxytryptamine 4
 agonist, on gastrointestinal contractile activity in
 conscious dogs.

AUTHOR(S): Haga, N.; Shiba, Y.; Mochiki, E.; Itoh, Z.
 CORPORATE SOURCE: GI Res. Labs., Inst. Molecular and Cellular Regulation,
 Gunma Univ., Maebashi, Japan
 SOURCE: Gastroenterology, (1995) Vol. 108, No. 4 SUPPL., pp. A609.
 Meeting Info.: 95th Annual Meeting of the American
 Gastroenterological Association and Digestive Disease Week.
 San Diego, California, USA. May 14-17, 1995.
 CODEN: GASTAB. ISSN: 0016-5085.

DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)

LANGUAGE: English
 ENTRY DATE: Entered STN: 9 Jun 1995
 Last Updated on STN: 11 Jul 1995

CONCEPT CODE: General biology - Symposia, transactions and proceedings
 00520
 Biochemistry methods - Proteins, peptides and amino acids
 10054
 Biochemistry studies - General 10060
 Biochemistry studies - Proteins, peptides and amino acids
 10064

Anatomy and Histology - Experimental anatomy 11104
 Anatomy and Histology - Surgery 11105
 Anatomy and Histology - Regeneration and transplantation 11107
 Movement 12100
 Pathology - Therapy 12512
 Metabolism - Proteins, peptides and amino acids 13012
 Digestive system - Physiology and biochemistry 14004
 Digestive system - Pathology 14006
 Nervous system - Anatomy 20502
 Nervous system - Physiology and biochemistry 20504
 Pharmacology - Drug metabolism and metabolic stimulators 22003
 Pharmacology - Clinical pharmacology 22005
 Pharmacology - Digestive system 22014

INDEX TERMS: Major Concepts
 Biochemistry and Molecular Biophysics; Digestive System (Ingestion and Assimilation); Metabolism; Morphology; Nervous System (Neural Coordination); Pharmacology; Physiology; Surgery (Medical Sciences)

INDEX TERMS: Chemicals & Biochemicals
 5-HYDROXYTRYPTAMINE; ACETYLCHOLINE

INDEX TERMS: Miscellaneous Descriptors
 ENDOGENOUS ACETYLCHOLINE RELEASE; GASTROINTESTINAL-DRUG; GASTROKINETIC AGENT; MEETING ABSTRACT; PHARMACODYNAMICS; TKS159; VAGAL DENERVATION; VAGOTOMY-ASSOCIATED DYSMOTILITY

ORGANISM: Classifier
 Canidae 85765
 Super Taxa
 Carnivora; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 Canidae
 Taxa Notes
 Animals, Carnivores, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates

REGISTRY NUMBER: 50-67-9 (5-HYDROXYTRYPTAMINE)
 51-84-3 (ACETYLCHOLINE)

L86 ANSWER 20 OF 22 USPATFULL on STN

ACCESSION NUMBER: 2005:324995 USPATFULL

TITLE: Non nucleoside reverse transcriptase inhibitors

INVENTOR(S): Deroy, Patrick, Laval, CANADA

Faucher, Anne-Marie, St-Placide, CANADA

Gagnon, Alexandre, Montreal, CANADA

Landry, Serge, St-Jerome, CANADA

Morin, Sebastien, Montreal, CANADA

O'Meara, Jeffrey, Boisbriand, CANADA

Simoneau, Bruno, Laval, CANADA

Thavonekham, Bounkham, Longueuil, CANADA

Yoakim, Christiane, Laval, CANADA

PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Ingelheim, GERMANY, FEDERAL REPUBLIC OF (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005282907	A1	20051222

APPLICATION INFO.: US 2005-137831 A1 20050524 (11)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2004-575888P	20040601 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	MICHAEL P. MORRIS, BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY RD, P O BOX 368, RIDGEFIELD, CT, 06877-0368, US	
NUMBER OF CLAIMS:	34	
EXEMPLARY CLAIM:	1	
LINE COUNT:	5025	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds of formula (I): ##STR1## wherein Ar, X, R.sup.1, R.sup.2, R.sup.3 and R.sup.4 are as defined herein. The compounds are useful as reverse transcriptase inhibitors against wild type and single or double mutant strains of HIV.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT	871473-74-4P	871473-75-5P	871473-76-6P	871473-77-7P	871473-78-8P
	871473-79-9P	871473-80-2P	871473-81-3P	871473-82-4P	871473-83-5P
	871473-84-6P	871473-85-7P	871473-86-8P	871473-87-9P	871473-88-0P
	871473-89-1P	871473-90-4P	871473-91-5P	871473-92-6P	871473-93-7P
	871473-94-8P	871473-95-9P	871473-96-0P	871473-97-1P	871473-98-2P
	871473-99-3P	871474-00-9P	871474-01-0P	871474-02-1P	871474-03-2P
	871474-04-3P	871474-05-4P	871474-06-5P	871474-07-6P	871474-08-7P
	871474-09-8P	871474-10-1P	871474-11-2P	871474-12-3P	871474-13-4P
	871474-14-5P	871474-15-6P	871474-16-7P	871474-17-8P	871474-18-9P
	871474-19-0P	871474-20-3P	871474-21-4P	871474-22-5P	871474-24-7P
	871474-26-9P	871474-27-0P	871474-28-1P	871474-29-2P	871474-30-5P
	871474-31-6P	871474-32-7P	871474-33-8P	871474-34-9P	871474-35-0P
	871474-36-1P	871474-37-2P	871474-38-3P	871474-39-4P	871474-40-7P
	871474-41-8P	871474-42-9P	871474-43-0P	871474-44-1P	871474-45-2P
	871474-46-3P	871474-47-4P	871474-48-5P	871474-49-6P	871474-50-9P
	871474-51-0P	871474-52-1P	871474-53-2P	871474-54-3P	871474-55-4P
	871474-56-5P	871474-57-6P	871474-58-7P	871474-59-8P	871474-60-1P
	871474-61-2P	871474-62-3P	871474-63-4P	871474-64-5P	871474-65-6P
	871474-66-7P	871474-67-8P	871474-68-9P	871474-69-0P	871474-70-3P
	871474-71-4P	871474-72-5P	871474-74-7P	871474-76-9P	871474-78-1P
	871474-80-5P	871474-82-7P	871474-83-8P	871474-84-9P	871474-85-0P
	871474-86-1P	871474-87-2P	871474-88-3P	871474-89-4P	871474-90-7P
	871474-91-8P	871474-92-9P	871474-93-0P	871474-94-1P	871474-95-2P
	871474-96-3P	871474-97-4P	871474-98-5P	871474-99-6P	871475-00-2P
	871475-01-3P	871475-02-4P	871475-03-5P	871475-04-6P	871475-05-7P
	871475-06-8P	871475-07-9P	871475-08-0P	871475-09-1P	871475-10-4P
	871475-11-5P	871475-12-6P	871475-13-7P	871475-14-8P	871475-15-9P
	871475-16-0P	871475-17-1P	871475-18-2P	871475-19-3P	871475-20-6P
	871475-21-7P	871475-22-8P	871475-23-9P	871475-24-0P	871475-25-1P
	871475-26-2P	871475-27-3P	871475-28-4P	871475-29-5P	871475-30-8P
	871475-31-9P	871475-32-0P	871475-33-1P	871475-34-2P	871475-35-3P
	871475-36-4P	871475-37-5P	871475-38-6P	871475-39-7P	871475-40-0P
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	871475-46-6P	871475-47-7P	871475-48-8P	871475-50-2P	871475-52-4P
	871475-54-6P	871475-56-8P	871475-58-0P	871475-60-4P	871475-62-6P
	871475-64-8P	871475-66-0P	871475-68-2P	871475-70-6P	871475-72-8P
	871475-74-0P	871475-75-1P	871475-76-2P	871475-77-3P	871475-78-4P
	871475-79-5P	871475-80-8P	871475-81-9P	871475-82-0P	871475-83-1P
	871475-84-2P	871475-85-3P	871475-86-4P	871475-87-5P	871475-88-6P
	871475-89-7P	871475-90-0P	871475-91-1P	871475-92-2P	871475-93-3P

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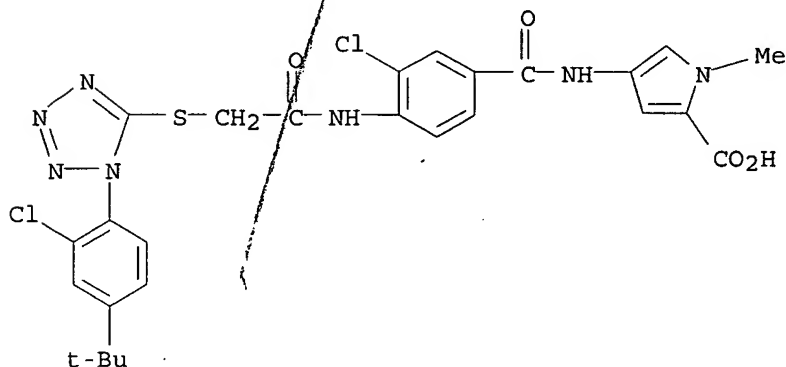
(drug candidate; preparation of acetamide derivs. as reverse transcriptase inhibitors for treatment of HIV infection)

IT 871475-96-6P

(drug candidate; preparation of acetamide derivs. as reverse transcriptase inhibitors for treatment of HIV infection)

RN 871475-96-6 USPATEFULL

CN 1H-Pyrrole-2-carboxylic acid, 4-[[[3-chloro-4-[[[1-[2-chloro-4-(1,1-dimethylethyl)phenyl]-1H-tetrazol-5-yl]thio]acetyl]amino]benzoyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



L86 ANSWER 21 OF 22 USPATEFULL on STN
 ACCESSION NUMBER: 2002:308379 USPATEFULL
 TITLE: Medicament
 INVENTOR(S): Skogvall, Staffan, Lund, SWEDEN

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002173505	A1	20021121
APPLICATION INFO.:	US 2001-984329	A1	20011029 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	SE 1999-1531	19990428
	SE 1999-1906	19990526
	SE 1999-2251	19990615
	SE 1999-2252	19990615
	WO 2000-SE819	20000428
	US 1999-131355P	19990428 (60)
	US 1999-136604P	19990527 (60)
	US 1999-139632P	19990617 (60)
	US 1999-139633P	19990617 (60)

DOCUMENT TYPE: Utility
 FILE SEGMENT: APPLICATION
 LEGAL REPRESENTATIVE: SMITH, GAMBRELL & RUSSELL, LLP, ATTORNEYS AT LAW, SUITE 800, 1850 M STREET, N.W., WASHINGTON, DC, 20036
 NUMBER OF CLAIMS: 14

EXEMPLARY CLAIM: 1
 LINE COUNT: 567

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A compound having agonist activity to the 5-HT.sub.4 receptor for use as a medicament and the use of said compound in the manufacture of a medicament for use in therapeutic or prophylactic treatment of disorders involving bronchocontraction of a human or animal body is described, as well as methods of treatment, wherein said compounds are administered. Further, a compound having antagonist activity to the 5-HT.sub.2a receptor for use as a medicament and the use of said compound in the manufacture of a medicament for use in therapeutic or prophylactic treatment of disorders involving bronchocontraction of a human or animal body is described, as well as methods of treatment, wherein said compounds are administered. Moreover, a composition comprising a combination of compounds comprising at least one compound with agonist activity to the 5-HT.sub.4 receptor agonist and at least one compound with antagonist activity to the 5-HT.sub.2, receptor antagonist is described, as well as such a composition for use as a medicament, the use of said composition for the manufacture of a medicament for therapeutic or prophylactic treatment of disorders involving bronchocontraction of a human or animal body, and methods of treatment, wherein said compositions are administered.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A compound having agonist activity to the 5-HT.sub.4 receptor for use as a medicament and the use of said compound in the manufacture of a medicament for use. . . described, as well as methods of treatment, wherein said compounds are administered. Further, a compound having antagonist activity to the 5-HT.sub.2a receptor for use as a medicament and the use of said compound in the manufacture of a medicament for use. . . are administered. Moreover, a composition comprising a combination of compounds comprising at least one compound with agonist activity to the 5-HT.sub.4 receptor agonist and at least one compound with antagonist activity to the 5-HT.sub.2, receptor antagonist is described, as well as such a composition for use as a medicament, the use of said composition. . .

SUMM [0002] The present invention relates to a compound having agonist activity to the 5-HT.sub.4 receptor for use as a medicament and to the use of said compound in the manufacture of a medicament for. . .

SUMM [0003] Receptors of the 5-HT (serotonin; 3-(P-aminoethyl)-5-hydroxyindole) type are well known and occur throughout the body, e.g. in the airways, and their relevance has mainly been reported in conjunction with treatment of CNS, muscle and gastric disorders, as disclosed in e.g. WO 98/18458 and U.S. Pat. No. 5,246,935. In such treatments, compounds having agonist activity to a 5-HT.sub.1 type receptor are often used. As examples of other 5-HT receptors, mention can be made of receptors of the 5-HT.sub.2, 5-HT.sub.4, 5-HT.sub.5, 5-HT₆ and 5-HT.sub.7 type. For a recent review of 5-HT receptors, see Gerhardt, C. C. van Heerikhuizen, H.; Eur. J. Phar., 334, 1-23 (1997), which is incorporated herein by reference.

SUMM [0004] Receptors of the 5-HT.sub.2 type are also well known, e.g. through U.S. Pat. Nos. 5,869,497, 5,705,519 and 5 246 935. The relevance of receptors of the 5-HT.sub.2 type has been reported in conjunction with e.g. CNS and neuronal disorders. Such disorders are often treated with compounds having

antagonist activity to a receptor of the .sup.5-HT .sub.2a, 5-HT.sub.2B or 5-HT .sub.2c type. Examples of such compounds are ritanserin and naftidroturyl. A review of typical agonists and antagonists of various 5-HT receptors is disclosed in R. A. Glennon, Neuroscience and Biobehavioral Reviews, 14, 35-47 (1990), the whole content of which is. . .

SUMM [0005] SU 1 701 320 A1 discloses the use of *serotonin* for treatment of acute asthma attacks. This reference does not suggest any receptor mechanism for *serotonin*, which is a compound with both a contracting and a relaxing effect on the airways, as is further discussed herein. . .

SUMM [0007] The present invention is based on the novel finding that certain 5-HT receptors are of utmost importance in regulating bronchocontraction. In summary, it is disclosed herein that compounds having agonist activity to the 5-HT.sub.4 receptor bring about a bronchorelaxing action upon administration thereof, and are therefore suitable as agents for treatment of bronchocontraction disorders. It is also disclosed herein that compounds having antagonist activity to the 5-HT.sub.2, especially 5-HT.sub.2a, receptor, are suitable agents in the treatment of bronchocontraction disorders. Methods for treatment of bronchocontraction disorders are also disclosed.

SUMM [0009] Accordingly, the present invention relates, in one of its aspects, to a compound having agonist activity to the 5-HT.sub.4 receptor for use as a medicament. In another aspect it relates to use of said compound in the manufacture of. . .

SUMM [0010] In a preferred embodiment, the invention relates to the use of a compound having agonist activity to the 5-HT.sub.4 receptor in the manufacture of a medicament for therapeutic or prophylactic treatment of disorders involving bronchocontraction, wherein said agonist has. . .

SUMM [0012] In a preferred embodiment, the invention relates to the use of a compound having antagonist activity to a 5-HT.sub.2, receptor in the manufacture of a medicament for therapeutic or prophylactic treatment of disorders involving bronchocontraction, wherein said antagonist has. . .

SUMM [0014] The present invention also relates to the use of a compound having antagonist activity to a 5-HT.sub.2a receptor in combination with a compound having agonist activity to the 5-HT.sub.4 receptor in the manufacture of a medicament for therapeutic or prophylactic treatment of disorders involving bronchocontraction. In a preferred embodiment said compound having agonist activity is *serotonin* or a derivative thereof having agonist activity to the 5-HT.sub.4 receptor. This combination of the 5-HT_{2a} receptor antagonist and the agonist increases the *serotonin* transmission in the body, particularly in the presence of a *serotonin* uptake inhibitor (SRI) - Further, the compounds having agonist activity to the 5-HT.sub.4 receptor to be used according to the present invention are also useful in the present combination embodiment. In particular, said. . .

SUMM [0015] According to the present invention several known substances are, surprisingly, able to stimulate the 5-HT.sub.4 receptor, without activating the contracting 5-HT .sub.2a receptor, thereby generating a relaxing effect on the bronchocontraction. Such agonist compounds are selected from the group comprising the substances. . .

SUMM [0023] According to the present invention several known antagonist compounds are, surprisingly, able to influence the 5-

*HT*2a receptor, thereby generating a contraction reducing effect, i.e. a relaxation effect, and are selected from a group comprising ketanserin, AMI-193.

SUMM . . . NE-100, Nefazodone, N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline, NRA0045, Olanzapine, Ondansetron, 1-(2-pyritnidinyl)piperazine derivatives, Pizotifen, raclopride, Roxindole, Risperidone, Ritanserin, RP62203, sarpogrelate and its active metabolite (M-1), *serotonin* reuptake inhibitors like fluoxetine, YM 992, medifoxamine, cericlamine, imipramine, iprindole, BIMT 17, citalopram, paroxetine, sertraline, fluvoxamine spiro indoles N-substituted with.

SUMM [0027] Ketanserin is excluded from the embodiment concerning the 5-*HT*.sub.2 receptor antagonist compound for use as a medicament.

SUMM . . . or animal patient a therapeutically effective amount of a compound according to the present invention having antagonist activity to a 5-*HT*.sub.2a receptor. Preferably, said method relates to treatment of asthma and disorders related thereto.

SUMM . . . the contraction in the airways caused (1) either by the underlying disease (asthma etc) or (2) by the administration of 5-*HT* or other substances with 5-*HT*.sub.2a-activating properties. The level of contraction in the airways can, for instance, be determined by spirometric measurements of the Forced Expiratory.

SUMM . . . As appears from FIG. 1, the contractile component often manifests itself as a reduction or a complete elimination of the 5-*HT* induced relaxation, rather than in an increase of force from the control (pre-exposure) level. In the case of "specific" agonists to the 5-*HT*.sub.4 receptor, this sustained relaxing effect is achieved because the contractile 5-*HT*2a receptor is not affected; only the relaxing 5-*HT*.sub.4 receptor is activated. In the case of antagonists to the 5-*HT*.sub.2a receptor, this effect is achieved due to direct blocking of the 5-*HT*.sub.2-, receptor, whereby the unspecific agonists to the 5-*HT*.sub.4 receptor, such as 5-*HT*, can act without also causing contraction by the 5-*HT*.sub.2, receptor.

SUMM . . . embodiment may optionally include two or more of the above outlined compounds, Further in the embodiment when the compound having 5-*HT*.sub.2, antagonist activity is administered, optionally together with complementary *serotonin* or derivatives thereof, a *serotonin* uptake inhibitor can be added with a view to amplifying the relaxing effect.

SUMM [0035] Said medicament may be prepared as a composition adapted either for administration via the respiratory tract or for oral, intravenous, topical, intraperitoneal or subcutaneous administration, in association with one or more pharmaceutically acceptable carriers, diluents or.

SUMM [0036] Moreover, said medicament is preferably administered via the respiratory tract in the form of e.g. an aerosol or an air-suspended fine powder. However, in some cases a useful alternative to administration via the respiratory tract may be oral, topical, parenteral, subcutaneous, transdermal or rectal administration, wherein e.g. tablets, capsules, powders, microparticles, granules, syrups, suspensions, . . .

SUMM [0037] FIG. 1 depicts the effects of 5-*HT* and selective 5-*HT*.sub.4 agonists on the spontaneous tone in human in vitro preparations. Note that 5-*HT* only gives a transient relaxation, while selective 5-*HT*.sub.4 agonists give a strong sustained relaxing effect.

- DETD [0040] Later experiments, not included in the thesis, have revealed that one of the regulating factors is *serotonin*, also called *5-HT*, which exerts agonist action on the receptors ceptors *5-HT.sub.4*, *5HT.sub.5*, *5-HT.sub.6*, *5-HT.sub.7* as well as on *5-HT.sub.2* receptors.
- DETD [0041] Additional experiments have shown that when 1 μ M *serotonin* was added to denuded airway smooth muscle preparations from the guinea-pig displaying a strong, smooth spontaneous tone, the average force level was increased significantly, i.e. a contraction was observed. A contractile effect of *serotonin* on airway smooth muscle has been reported in e.g. SkQgvall, S., Korsgren, M-, Grampp, W., J. Appl. Phys., 86:789-798, 1999. However, when 10 μ M of *serotonin* was added, the spontaneous tone was significantly suppressed to a level of about half the force observed in control (drug-free). . . its normal level when the preparations were again exposed to control conditions. Thus, it has now surprisingly been shown that *serotonin* brings about contraction of the airways at low concentrations and relaxation at high concentrations, consequently having a dual effect on. . .
- DETD [0042] Furthermore, it has been shown that when the contracting *5-HT2*, receptor was blocked with ketanserin, the S-ST, i.e. *serotonin*, induced almost no contraction, but instead only a significant relaxation. Similar experiments have also been performed on human in vitro preparations, from patients undergoing lobectomy or pulmectomy due to lung cancer. It was found that in this tissue, *5-HT* was even more potent in relaxing the airway smooth muscle than in guinea pig. In human tissue, already 1 μ M *5-HT* induces a significant relaxation of the spontaneous tone.
- DETD . . . a weak contraction when exposed to S-HT. Nevertheless, examinations on spontaneous tone on human in vitro preparations have shown that *5-HT* indeed has a contractile component also in this tissue. However, this contraction takes a longer time to develop than in. . . 1). The transient nature of the 5-ET relaxation is most likely caused by a simultaneous activation of the fast, relaxing *5-HT.sub.4* receptor, and a slower activation of the contracting SHT.sub.2a receptor. This is clear, because activation of the relaxing *5-HT.sub.4* receptor by a Substance that lacks *5-HT.sub.2*, receptor activating properties (such as 5-carboxiamidotryptamine or SC 53116), results in a relaxation that is persistent and not transient (see. . .
- DETD . . . be useful in the treatment of bronchoobstructive diseases. In SU 1 701 320 it is suggested that the 5-Hr.sub.1 i.e. *serotonin*, may be of use as an addition to standard beta2 receptor stimulation. However, from our experiments it seems clear that. . . asthmatic disorders, because of the transient relaxing effect by S-HrT (see FIG. 1). If instead, as we propose herein, a *5-HT* analogue that lacks the *5-HT2a* activating properties is given, the relaxing effect is persistent, and not transient.
- DETD [0045] In summary, it has now been discovered that agonist action on the *5-HT.sub.4* receptor results in a relaxing effect, whereas agonist action on *5-HT2a* receptors results in a contractile effect. In conclusion, the dual effect of *serotonin* is most likely a result of its agonist action on the relaxing 5-UT.sub.4 receptor as well as on the contracting 5-HT.sub.27 receptor.
- DETD [0046] It was also deduced from these experiments that compounds having agonist activity to the *5-HT.sub.4* receptor, while having only low or no agonist activity to a *5-HT*

.sub.2a receptor, therefore are useful as agents for treatment of bronchocontraction disorders.

DETD [0047] Thus, the present invention relates to the use of compounds having agonist activity to the 5-HT.sub.4 receptor in the manufacture of a medicament intended for treatment of bronchocontraction disorders, whereby said compounds have the strong bronchorelaxing effect of *serotonin* but have substantially no contractile effect. As mentioned above, the compounds used according to the present invention have only low or no agonist activity to 5-HT.sub.2a receptors.

DETD [0048] In the above mentioned experiments it has also been shown that compounds having antagonist activity to a 5-HT₂ receptor are useful as agents for treatment of bronchocontraction disorders, since they are capable of blocking the contractile effect of a compound having agonist activity to a 5-HT.sub.2, receptor. The compounds according to the present invention having antagonist activity to the 5-HT.sub.2, receptor may even be administered together with *serotonin* in the form of a complement so the *serotonin* content already present in the body with a view to obtaining an amplified contracting effect, or with any other substance having agonist activity to the 5-HT_{2a} receptor; or with a *serotonin* uptake inhibitor. Said administration can be simultaneous or sequential, and a powerful relaxing effect on the bronchi can be achieved. . . . this manner. Thus, the present invention also relates to the combined use of a compound having antagonist activity to a 5-HT₂ receptor and a compound having agonist activity to the 5-HT.sub.4 receptor, in the manufacture of a medicament for therapeutic or prophylactic treatment of disorders involving bronchocontraction.

CLM What is claimed is:

1. Use of one or more compounds having antagonist activity to a 5-HT₁ receptor, and derivatives and pharmaceutically acceptable salts thereof having antagonist activity to the 5-HT.sub.2. receptor in the manufacture of a medicament for therapeutic or prophylactic treatment of disorders involving human bronchocontraction chosen from the
 Nefazodone, N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline, NRA0045, olanzapine, Ondansetron, 1-(2-pyrimidinyl) piperazine derivatives, Pizotifen, raclopride, Roxindole, Risperidone, Ritanserin, RP62203, sarpogrelate and its active metabolite (M-1), *serotonin* reuptake inhibitors like fluoxetine, YM 992, medetoxamine, cericlamine, imipramine, iprindole, BIMT 17, citalopram, paroxetine, sertraline, fluvoxamine Spiro indoles N-substituted with. . . .
6. Use of one or more compounds having agonist activity to a 5-HT.sub.4 receptor in the manufacture of a medicament for therapeutic or prophylactic treatment of disorders involving human bronchocontraction, chosen from the
10. Use of a composition comprising a combination of at least one compound with agonist activity to the 5-HT-.sub.4 receptor, and at least one compound with antagonist activity to the 5-HT_{2a} receptor for the manufacture of a medicament for therapeutic or prophylactic treatment of disorders involving bronchocontraction, chosen from the group. . . .
 least 60%, and most preferably at least 90%, and wherein said combination is chosen from the following groups of a) 5-HT.sub.4 receptor agonists, and b) 5-HT.sub.2. receptor antagonists, or derivatives or pharmaceutically acceptable salts thereof: a) 5-HT.sub.4 receptor agonists: 5-carboxamidotryptamine, LIMU 1, BIMU 8, BRL 24924, Cisapride,

DAU 6236, 5-hydroxy-N,N-dimethyltryptamin, ML-1035, ML 10302, 5-metoxytryptamin, Metoclopramide, Mosapride, 8-OH-DPAT. . . 216-454, SR59768, TKS159, VB20B7, YM-4781,3, YM-53389, S YM-09151, Zacopride, Zelmec, arylcarbamate derivatives of 1-piperidineethanol, 2-piperazinylbenzoxazole derivatives, clebopride, and ##STR10## and **serotonin (5-HT)** and derivatives and pharmaceutically acceptable salts thereof. b) S-HT.sub.2a receptor antagonists: AMI-193 and MDL 100,907, ALEPH-2, Amperozide, amesergide, aryloxyalkylimidazolines, 1-aryl-4-propylpiperazines, . . . Nefazodone, N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline, NRA0045, Olanzapine, Ondansetron, 1-(2-pyrimidinyl) piperazine derivatives, Pizotifen, raclopride, Roxindole, Risperidone, Ritanserin, RP62203, sarpogrelate and its active metabolite (M-1), **serotonin** reuptake inhibitors like fluoxetine, YM 992, medifoxamine, cericlamine, imipramine, iprindole, BIMT 17, citalopram, paroxetine, sertraline, fluvoxamine spiro indoles N-substituted with. . .

12. Use according to claim 11, wherein the composition comprises the following combinations of a 5-HT.sub.4 receptor agonist and a 5-HT.sub.2, receptor antagonist: VB20B7 and AMI-193, VB20B7 and MDL 11939, RS67333 and AMI-193, RS67333 and MDL 11939, VB20B7 and WAY 100635, . . .

. . . obstructive pulmonary disease, wherein said method comprises administering to a human or animal patient a therapeutically effective amount of a 5-HT.sub.4 receptor agonist according to any one of claims 6 and 7 and a 5-HT.sub.2a receptor antagonist according to any one of claims 1-3, either simultaneously or sequentially.

IT 50-37-3, LSD 50-49-7, Imipramine 50-67-9D, Serotonin, derivs. 110-85-0D, Piperazine, aryl derivs., biological studies 129-03-3, Cyproheptadine 361-37-5, Methysergide 364-62-5, Metoclopramide 487-93-4, 5-Hydroxy-N,N-dimethyltryptamine 510-74-7, AMI-193 548-43-6, Elymoclavine 608-07-1, 5-Methoxytryptamine 749-02-0, Spiperone 4205-90-7, Clonidine 5560-72-5, Iprindole 15574-96-6, Pizotifen 16357-59-8, N-Ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline 17692-51-2, Metergoline 20980-22-7D, 1-(2-Pyrimidinyl)piperazine, derivs. 24219-97-4, Mianserin 28299-33-4D, Imidazoline, aryloxyalkyl derivs. 32359-34-5, Medifoxamine 32896-53-0, LY 53857 free base 54739-18-3, Fluvoxamine 54910-89-3, Fluoxetine 59729-33-8, Citalopram 61869-08-7, Paroxetine 64795-35-3, Mesulergine 67537-81-9D, Hexahydrocarbazole, derivs. 74050-98-9, Ketanserin 74885-09-9, 5-Carboxamidotryptamine 75272-39-8, YM 09151 75558-90-6, Amperozide 78950-78-4, 8-OH-DPAT 79617-96-2, Sertraline 81098-60-4, Cisapride 83366-66-9, Nefazodone 84225-95-6, Raclopride 84625-59-2, Dotarizine 85273-96-7, ICI 169369 87051-43-2, Ritanserin 90182-92-6, Zacopride 99614-02-5, Ondansetron 99746-68-6, (R,R)-LY-53857 99746-70-0, (S,R)-LY-53857 99746-72-2, (R,S)-LY-53857 100746-36-9, CGS 18102A 100762-72-9, (S,S)-LY-53857 106266-06-2, Risperidone 107703-78-6, MDL 11939 109872-41-5, BRL 24924 112192-04-8, Roxindole 112727-80-7, Renzapride 112885-41-3, Mosapride 112922-55-1, Cericlamine 120444-71-5, Deramciclanc 121588-75-8, Amesergide 122866-79-9, R 076186 125557-35-9 125926-17-2, Sarpogrelate 127266-56-2, WY 50324 127595-11-3, DAU 6236 127595-43-1, BIMU 1 127625-29-0, Fananserin 130580-02-8, SR 46349B 132539-06-1, Olanzapine 133364-63-3, DV 7028 134296-40-5, BIMU 8 136861-96-6, MDL 28133A 137328-52-0, LY 215840 138752-34-8, RS 56532 139290-65-6, MDL 100907 139290-69-0, MDL 100151 141196-99-8, SC-53116 142228-17-9, TKS 159 146388-57-0, SC-49518 146714-97-8, WAY 100635 146714-97-8D, WAY 100635, derivs. 146715-07-3, Desmethyl-WAY 100635 148702-58-3, SB 204070 148868-55-7, ML 10302 149409-57-4 150527-23-4 150527-36-9, FG5893 hydrochloride

10/27/2006

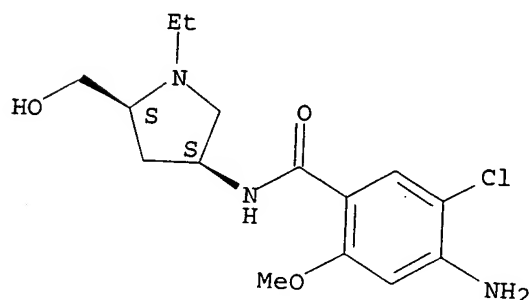
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 RS 67532 166743-12-0, SK-951 166815-18-5, RS 17017 167933-07-5,
 BIMT 17 168986-60-5, RS 67333 168986-61-6, RS 67506 169789-38-2,
 SDZ 216-454 172679-55-9, SR59768 175413-81-7, SB 205149
 178485-02-4, ALEPH-2 179474-80-7, R 093877 179474-81-8, Prucalopride
 183949-64-6, NRA0045 189188-57-6, Zelmec 193404-36-3, RS 57639
 208661-17-0, LU 111995 217635-62-6 217635-64-8 220850-98-6, YM
 53389 303953-05-1 303953-06-2 303955-07-9, YM 47813

(serotonergic agonists and antagonists for treatment of
 bronchoconstriction-related disorders)

IT 142228-17-9, TKS 159
 (serotonergic agonists and antagonists for treatment of
 bronchoconstriction-related disorders)

RN 142228-17-9 USPTAFULL
 CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-
 pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L86 ANSWER 22 OF 22 USPTAFULL on STN
 ACCESSION NUMBER: 92:72489 USPTAFULL
 TITLE: Benzamide derivatives
 INVENTOR(S): Fujiwara, Hiromichi, Hyogo, Japan
 Ogawa, Akihiko, Hyogo, Japan
 Sakiyama, Hideyo, Hyogo, Japan
 Tamura, Toshiaki, Hyogo, Japan
 PATENT ASSIGNEE(S): Teikoku Chemical Industry Co., Ltd., Osaka, Japan
 (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5143935		19920901
APPLICATION INFO.:	US 1991-777011		19911016 (7)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1990-277976	19901016
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Lee, Mary C.	
ASSISTANT EXAMINER:	McKane, Joseph K.	
LEGAL REPRESENTATIVE:	Wenderoth, Lind & Ponack	
NUMBER OF CLAIMS:	5	
EXEMPLARY CLAIM:	1	
LINE COUNT:	723	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A benzamide derivative represented by the formula: ##STR1## having a

Searched by John DiNatale x2-2557

promoting activity of **gastrointestinal tract** and pharmaceutical composition containing the same.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A benzamide derivative represented by the formula: ##STR1## having a promoting activity of **gastrointestinal tract** and pharmaceutical composition containing the same.

SUMM The present invention relates to a class of novel benzamide derivatives each having a promoting activity to **gastrointestinal tract**.

SUMM 4-Amino-5-chloro-N-((2-diethylamino) ethyl)-2-methoxy benzamide (common name: Metoclopramide) is a well-known compound having a promoting activity to **gastrointestinal tract** and especially to **stomach**, and (±) 4-amino-5-chloro-N-(3R*,4S*)-1-(3-(p-fluorophenoxy)propyl)-3-methoxy-4-piperidyl)-o-anisamide (common name: Cisapride) is a well-known **gastrokinetic** compound customarily used for the treatment of chronic **gastrics**, syndrome of **gastrointestinal tract** accompanied with **postgastrectomy**, regurgitant esophagitis and suprious obstipation. Metoclopramide has, however, undesired properties of inducing extrapyramidal syndrome and other undesired syndrome; due to.

SUMM Under the circumstances, it has long been desired to have a new medicinal compound which is excellent in absorption through **gastrointestinal tract** and has the least activity toward central nervous system.

SUMM . . . class of compounds having no or substantially no activity toward central nervous system and having an excellent promoting activity to **digestive tract** and especially to **stomach**

SUMM Thus obtained compounds of the present invention are characterized in that they have excellent promoting activities to **digestive tract** and especially to **stomach**, but no or substantially no activities toward central nervous system.

SUMM (1) Promoting activity to **gastric** emptying:

SUMM . . . 0.1 ml of aqueous 1.5% carboxymethyl cellulose solution containing 0.05% phenol red was orally administered. After leaving for 15 minutes, **stomach** was extracted and the phenol red amount remaining in the **stomach** was measured to determine the excreting activity for the tested compound.

DETD The present benzamide derivatives each has the properties for promoting activity to **digestive tract** and especially to **stomach**.

DETD In mouse tests, **stomach** excretion promoting rates of the compounds obtained in Examples 11 to 15 were 21.1% at the dosis of 0.3 mg/kg, . . .

DETD . . . TABLE 1

Promoting rate (%) of prevention of stomach excretion in mouse vomiting in dog		
Example at 3 mg/kg (p.o.) at 0.1 mg/kg (s.c.)		
1	42	no
2	37	no
3	36	no
4		

DETD . . . TABLE 2

Promoting rate (%)
 prevention of
 stereo- of stomach excretion
 vomiting
 specf. in mouse at 3 mg/kg
 in dog at 0.1 mg/kg
 Example
 struct. (p.o.) (s.c.)

11	2'S,4'S	42.8	no
16	2'R,4'R	20.0	no
17	2'S,4'R	10.6	no
18	2'R,4'S	22.3	no

Stomach excretion activities of Metoclopramide
 and Cisapride in mouse are as follows:

Metoclopramide	0.3 mg/kg	8.3%
	1.0	9.4
	3.0	25.0
	10.0	34.8
	30.0	

CLM What is claimed is:

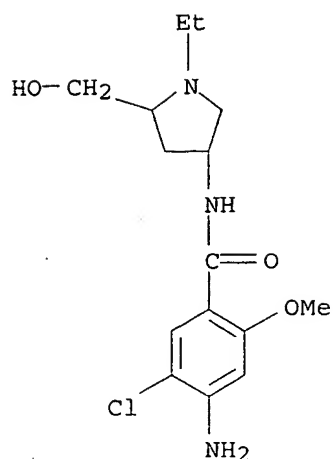
4. A pharmaceutical composition comprising an effective amount for promoting activities of the *gastrointestinal tract* of derivative of the formula: ##STR10## or its acid addition salt, in which R.sub.1 is hydrogen atom, lower alkyl, halogen.
5. A method for promoting activity of the *gastrointestinal tract* which comprises administering an effective amount of a benzamide derivative as defined in claim 1.

IT 142228-16-8P 142228-17-9P 142228-18-0P
 142228-19-1P 142228-20-4P 142228-21-5P
 142347-67-9P 142347-68-0P 142347-69-1P
 142347-70-4P 142347-71-5P 142347-72-6P
 142347-73-7P 142347-74-8P 142347-75-9P
 142347-76-0P 142347-77-1P 142347-78-2P
 142347-79-3P 142347-80-6P
 (preparation of, as gastric motility promoter)

IT 142228-16-8P 142228-17-9P 142228-18-0P
 142228-19-1P 142228-20-4P 142228-21-5P
 142347-67-9P 142347-68-0P 142347-69-1P
 142347-70-4P 142347-71-5P 142347-72-6P
 142347-73-7P 142347-74-8P 142347-75-9P
 142347-76-0P 142347-77-1P 142347-78-2P
 142347-79-3P 142347-80-6P
 (preparation of, as gastric motility promoter)

RN 142228-16-8 USPATFULL

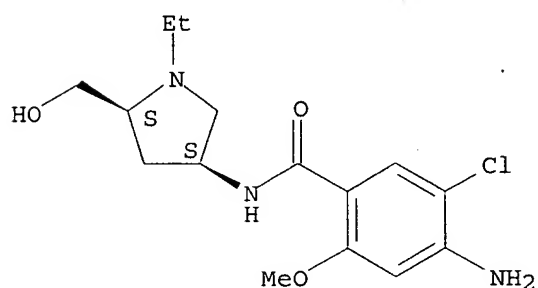
CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)



RN 142228-17-9 USPATFULL

CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

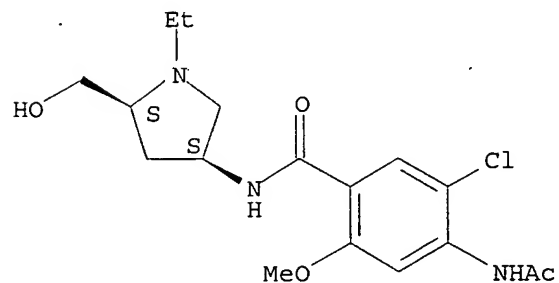
Absolute stereochemistry.



RN 142228-18-0 USPATFULL

CN Benzamide, 4-(acetylamino)-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, (3S-cis)- (9CI) (CA INDEX NAME)

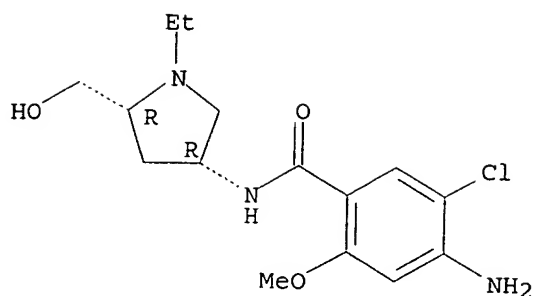
Absolute stereochemistry.



RN 142228-19-1 USPATFULL

CN Benzamide, 4-amino-5-chloro-N-[(3R,5R)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

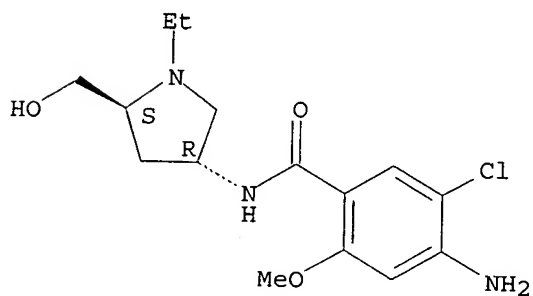
Absolute stereochemistry.



RN 142228-20-4 USPATFULL

CN Benzamide, 4-amino-5-chloro-N-[(3R,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

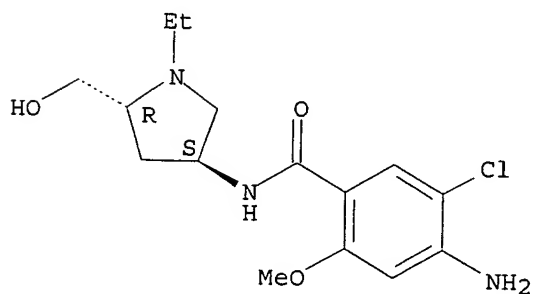
Absolute stereochemistry.



RN 142228-21-5 USPATFULL

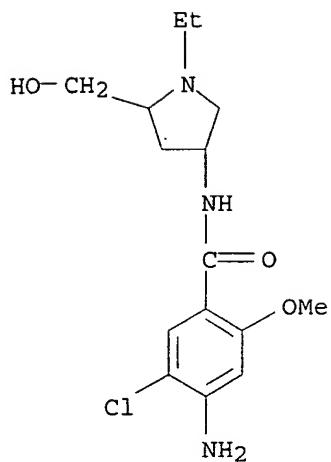
CN Benzamide, 4-amino-5-chloro-N-[(3S,5R)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 142347-67-9 USPATFULL

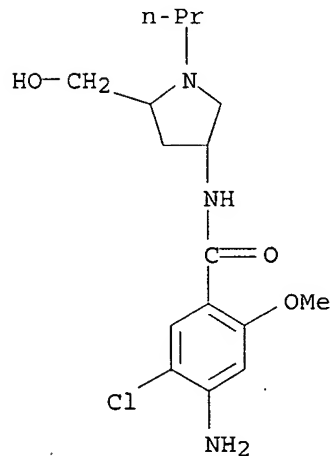
CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 142347-68-0 USPATFULL

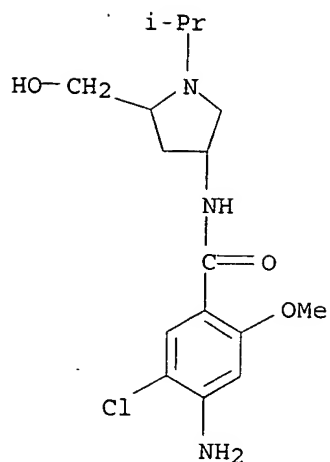
CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-propyl-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 142347-69-1 USPATFULL

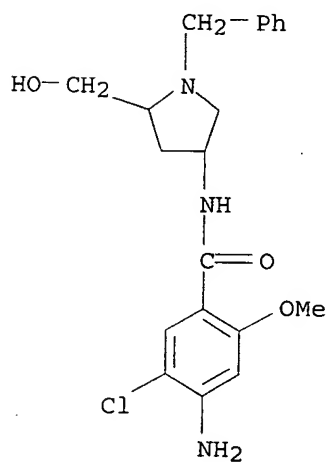
CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-(1-methylethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 142347-70-4 USPATFULL

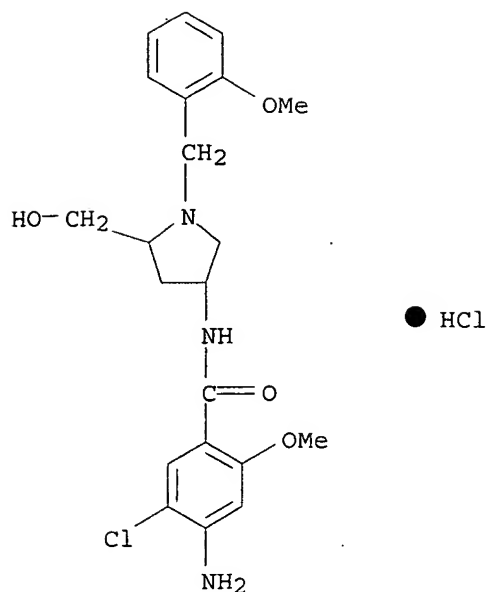
CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-(phenylmethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

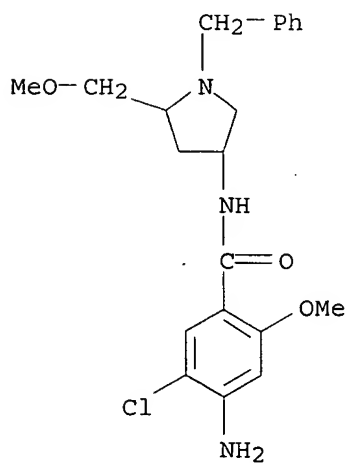
RN 142347-71-5 USPATFULL

CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-[(2-methoxyphenyl)methyl]-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



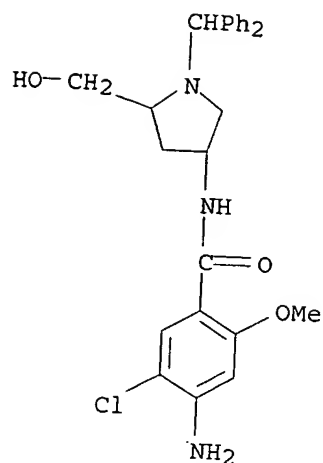
RN 142347-72-6 USPATFULL

CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[5-(methoxymethyl)-1-(phenylmethyl)-3-pyrrolidinyl]-, monohydrochloride (9CI) (CA INDEX NAME)



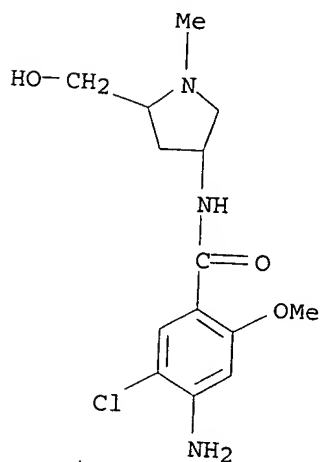
RN 142347-73-7 USPATFULL

CN Benzamide, 4-amino-5-chloro-N-[1-(diphenylmethyl)-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



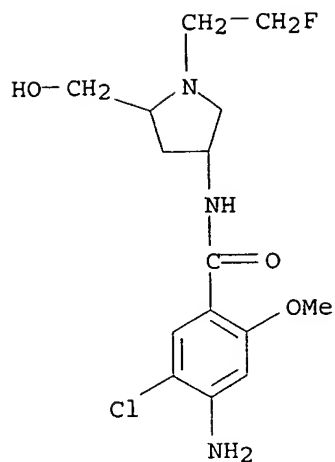
● HCl

RN 142347-74-8 USPATFULL
 CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-methyl-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



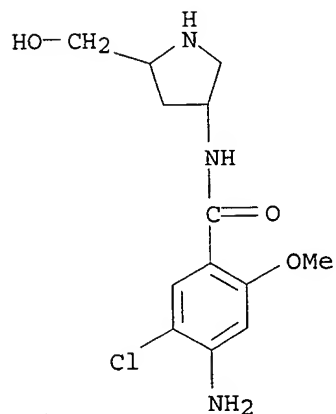
● HCl

RN 142347-75-9 USPATFULL
 CN Benzamide, 4-amino-5-chloro-N-[1-(2-fluoroethyl)-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

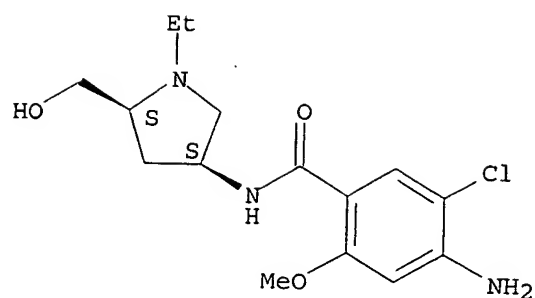
RN 142347-76-0 USPATFULL
 CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-
 , monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 142347-77-1 USPATFULL
 CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-
 methoxy-, monohydrochloride, (3S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

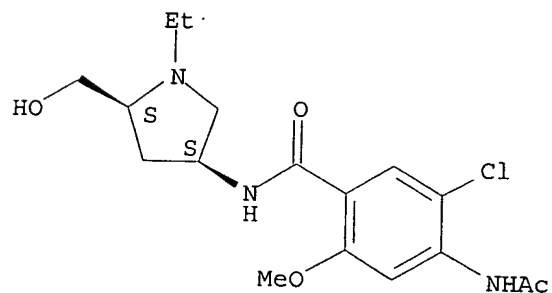


● HCl

RN 142347-78-2 USPATFULL

CN Benzamide, 4-(acetylamino)-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride, (3S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

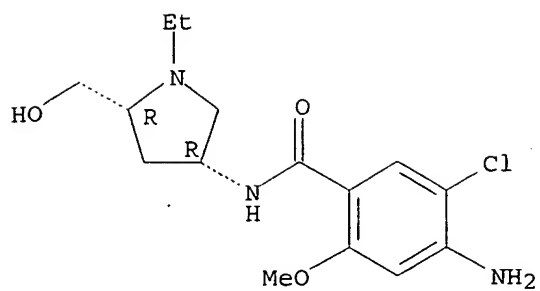


● HCl

RN 142347-79-3 USPATFULL

CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride, (3R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

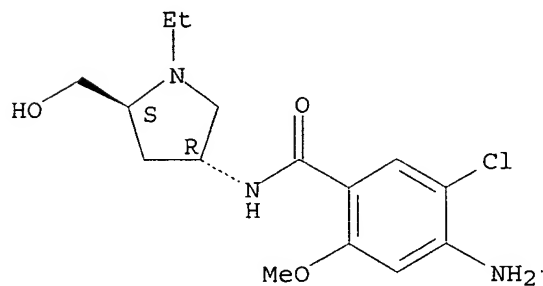


● HCl

RN 142347-80-6 USPATFULL

CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride, (3R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

=> d his full

(FILE 'HOME' ENTERED AT 12:40:28 ON 26 OCT 2006)

FILE 'CAPLUS' ENTERED AT 12:40:34 ON 26 OCT 2006
E US2005-526780/APPS

L1 1 SEA ABB=ON PLU=ON US2005-526780/AP
D SCA
SEL RN

FILE 'REGISTRY' ENTERED AT 12:41:00 ON 26 OCT 2006

L2 9 SEA ABB=ON PLU=ON (24201-13-6/BI OR 33996-28-0/BI OR
33996-30-4/BI OR 672285-79-9/BI OR 672285-80-2/BI OR 672285-81-
3/BI OR 672285-82-4/BI OR 672285-83-5/BI OR 672285-84-6/BI)
D SCA

FILE 'STNGUIDE' ENTERED AT 12:44:26 ON 26 OCT 2006

FILE 'REGISTRY' ENTERED AT 12:53:56 ON 26 OCT 2006
STRUCTURE UPLOADED

L3 4 SEA SSS SAM L3
L4 D SCA

L5 STRUCTURE UPLOADED

L6 4 SEA SSS SAM L5

L7 47 SEA SSS FUL L5

SAVE TEMP L7 SPI780STR7L/A

FILE 'CAPLUS' ENTERED AT 12:59:24 ON 26 OCT 2006

L8 18 SEA ABB=ON PLU=ON L7
L9 1 SEA ABB=ON PLU=ON L8 AND L1
D SCA
SEL HIT RN

FILE 'REGISTRY' ENTERED AT 13:01:16 ON 26 OCT 2006

L10 2 SEA ABB=ON PLU=ON (672285-79-9/BI OR 672285-84-6/BI)

FILE 'REGISTRY' ENTERED AT 13:01:41 ON 26 OCT 2006
D IDE L10 1-2

FILE 'CAPLUS' ENTERED AT 13:03:06 ON 26 OCT 2006
D SCA L8

L11 105205 SEA ABB=ON PLU=ON ?STOMACH?/BI
L12 42051 SEA ABB=ON PLU=ON ?MOTIL?/BI
L13 4188 SEA ABB=ON PLU=ON ?PERISTAL?/BI
L14 249583 SEA ABB=ON PLU=ON ?DIGEST?/BI
L*** DEL 199220 S ?INTESTIN?
L15 288318 SEA ABB=ON PLU=ON ?INTESTIN?/BI
L16 43191 SEA ABB=ON PLU=ON (5HT OR 5 HT?)/BI
L17 77545 SEA ABB=ON PLU=ON ?SEROTONIN?/BI
L18 22550 SEA ABB=ON PLU=ON ?ILEUM?/BI
L19 18576 SEA ABB=ON PLU=ON ?JEJUN?/BI
L20 31539 SEA ABB=ON PLU=ON ?DUODEN?/BI
L21 139482 SEA ABB=ON PLU=ON TRACT#/BI
L22 171670 SEA ABB=ON PLU=ON ?GASTR?/BI
L23 12 SEA ABB=ON PLU=ON L8 AND (L11 OR L12 OR L13 OR L14 OR L15 OR
L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22)
L24 162 SEA ABB=ON PLU=ON KITAJIMA A?/AU
L25 3 SEA ABB=ON PLU=ON AKIHIKO K?/AU
L26 5 SEA ABB=ON PLU=ON KAMODA O?/AU

L27 22 SEA ABB=ON PLU=ON OSAMU K?/AU
 E KAMODA/AU
 L28 6 SEA ABB=ON PLU=ON OHSAKO A?/AU
 L29 2 SEA ABB=ON PLU=ON AKIHIRO O?/AU
 L30 574 SEA ABB=ON PLU=ON YANAGI T?/AU
 L31 1 SEA ABB=ON PLU=ON TOSHIHARU Y?/AU
 L32 165 SEA ABB=ON PLU=ON (L24 OR L25)
 L33 27 SEA ABB=ON PLU=ON (L26 OR L27)
 L34 8 SEA ABB=ON PLU=ON (L28 OR L29)
 L35 575 SEA ABB=ON PLU=ON (L30 OR L31)
 L36 1 SEA ABB=ON PLU=ON L32 AND (L33 OR L34 OR L35)
 L37 5 SEA ABB=ON PLU=ON L33 AND (L34 OR L35)
 L38 1 SEA ABB=ON PLU=ON L34 AND L35
 L39 5 SEA ABB=ON PLU=ON (L36 OR L37 OR L38)
 L40 3 SEA ABB=ON PLU=ON (L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR
 L30 OR L31) AND (L23 OR L8)

FILE 'MEDLINE' ENTERED AT 13:14:46 ON 26 OCT 2006

L41 235 SEA ABB=ON PLU=ON (L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR
 L30 OR L31)
 L42 2 SEA ABB=ON PLU=ON (L36 OR L37 OR L38)

FILE 'REGISTRY' ENTERED AT 13:16:02 ON 26 OCT 2006

L43 SET SMARTSELECT ON
 SEL PLU=ON L7 1- CHEM : 49 TERMS
 SET SMARTSELECT OFF

FILE 'MEDLINE' ENTERED AT 13:16:05 ON 26 OCT 2006

L44 3 SEA ABB=ON PLU=ON L43
 D SCA
 D TRIAL 1-3
 D QUE L44
 D L43
 D L43 1-49
 L45 0 SEA ABB=ON PLU=ON FAUC65
 L46 5 SEA ABB=ON PLU=ON TKS159
 D TRIAL 1-5
 L47 1149902 SEA ABB=ON PLU=ON (L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR
 L17 OR L18 OR L19 OR L20 OR L21 OR L22)
 L48 5 SEA ABB=ON PLU=ON L47 AND ((L44 OR L45 OR L46))
 L49 2 SEA ABB=ON PLU=ON L41 AND (L44 OR L46 OR L48)

FILE 'EMBASE' ENTERED AT 13:20:17 ON 26 OCT 2006

L50 198 SEA ABB=ON PLU=ON (L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR
 L30 OR L31)
 L51 2 SEA ABB=ON PLU=ON (L36 OR L37 OR L38)

FILE 'REGISTRY' ENTERED AT 13:20:54 ON 26 OCT 2006

L52 SET SMARTSELECT ON
 SEL PLU=ON L7 1- CHEM : 49 TERMS
 SET SMARTSELECT OFF

FILE 'EMBASE' ENTERED AT 13:20:56 ON 26 OCT 2006

L53 7 SEA ABB=ON PLU=ON L52
 L54 4 SEA ABB=ON PLU=ON FAUC65 OR TKS159
 L55 7 SEA ABB=ON PLU=ON (L53 OR L54)
 L56 7 SEA ABB=ON PLU=ON (L53 OR L54) AND (L11 OR L12 OR L13 OR L14
 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22)
 D TRIAL 1-7
 L57 2 SEA ABB=ON PLU=ON L50 AND (L53 OR L54 OR L56)

FILE 'BIOSIS' ENTERED AT 13:25:28 ON 26 OCT 2006
 L58 252 SEA ABB=ON PLU=ON (L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR
 L30 OR L31)
 L59 4 SEA ABB=ON PLU=ON (L36 OR L37 OR L38)

FILE 'REGISTRY' ENTERED AT 13:25:56 ON 26 OCT 2006
 SET SMARTSELECT ON
 L60 SEL PLU=ON L7 1- CHEM : 49 TERMS
 SET SMARTSELECT OFF

FILE 'BIOSIS' ENTERED AT 13:25:57 ON 26 OCT 2006
 L61 3 SEA ABB=ON PLU=ON L60
 L62 5 SEA ABB=ON PLU=ON FAUC65 OR TKS159
 L63 2 SEA ABB=ON PLU=ON L58 AND (L61 OR L62)

FILE 'REGISTRY' ENTERED AT 13:27:39 ON 26 OCT 2006
 L64 1 SEA ABB=ON PLU=ON FAUC 65/CN
 L65 1 SEA ABB=ON PLU=ON TKS 159/CN
 D SCA
 D SCA L64
 SEL RN L10
 SEL RN L64
 SEL RN L65
 L66 1 SEA ABB=ON PLU=ON (672285-79-9/CRN OR 672285-84-6/CRN OR
 627529-76-4/CRN OR 142228-17-9/CRN)
 D SCA
 D IDE L64
 D IDE L65
 D IDE L66
 D STAT QUE L7
 L67 4 SEA ABB=ON PLU=ON L65 OR L66 OR L10
 D SCA

FILE 'USPATFULL, USPAT2' ENTERED AT 13:39:42 ON 26 OCT 2006
 L68 3 SEA ABB=ON PLU=ON L67
 D SCA
 L69 4 SEA ABB=ON PLU=ON L7
 L70 308291 SEA ABB=ON PLU=ON (L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR
 L17 OR L18 OR L19 OR L20 OR L21 OR L22)
 L71 3 SEA ABB=ON PLU=ON L69 AND L70
 L72 183 SEA ABB=ON PLU=ON L41
 L73 7 SEA ABB=ON PLU=ON L42
 L74 1 SEA ABB=ON PLU=ON L72 AND (L69 OR L71)

FILE 'STNGUIDE' ENTERED AT 13:42:37 ON 26 OCT 2006

FILE 'REGISTRY' ENTERED AT 13:45:53 ON 26 OCT 2006
 D STAT QUE L7

FILE 'CAPLUS' ENTERED AT 13:45:54 ON 26 OCT 2006
 D QUE NOS L39
 D QUE NOS L40
 L75 6 SEA ABB=ON PLU=ON L39 OR L40

FILE 'MEDLINE' ENTERED AT 13:45:58 ON 26 OCT 2006
 D QUE NOS L42
 D QUE NOS L49
 L76 3 SEA ABB=ON PLU=ON L42 OR L49

FILE 'EMBASE' ENTERED AT 13:46:01 ON 26 OCT 2006
 D QUE NOS L51
 D QUE NOS L57
 L77 3 SEA ABB=ON PLU=ON L51 OR L57

FILE 'BIOSIS' ENTERED AT 13:46:04 ON 26 OCT 2006
 D QUE NOS L59
 D QUE NOS L63
 L78 5 SEA ABB=ON PLU=ON L59 OR L63

FILE 'USPATFULL, USPAT2' ENTERED AT 13:46:07 ON 26 OCT 2006
 D QUE NOS L73
 D QUE NOS L74
 L79 7 SEA ABB=ON PLU=ON L73 OR L74

FILE 'STNGUIDE' ENTERED AT 13:46:29 ON 26 OCT 2006

FILE 'CAPLUS, MEDLINE, EMBASE, BIOSIS, USPATFULL, USPAT2' ENTERED AT
 13:46:50 ON 26 OCT 2006
 L80 12 DUP REM L75 L76 L77 L78 L79 (12 DUPLICATES REMOVED)
 ANSWERS '1-6' FROM FILE CAPLUS
 ANSWERS '7-9' FROM FILE BIOSIS
 ANSWERS '10-12' FROM FILE USPATFULL
 D IBIB ABS HITIND HITSTR L80 1-6
 D IALL L80 7-9
 D IBIB ABS KWIC HITSTR L80 10-12

FILE 'REGISTRY' ENTERED AT 13:51:05 ON 26 OCT 2006
 D STAT QUE L7

FILE 'CAPLUS' ENTERED AT 13:51:07 ON 26 OCT 2006
 D QUE NOS L8
 D QUE NOS L23
 L81 15 SEA ABB=ON PLU=ON (L8 OR L23) NOT L75

FILE 'MEDLINE' ENTERED AT 13:51:10 ON 26 OCT 2006
 D QUE NOS L44
 D QUE NOS L46
 D QUE NOS L48
 L82 3 SEA ABB=ON PLU=ON (L44 OR L46 OR L48) NOT L76

FILE 'EMBASE' ENTERED AT 13:51:14 ON 26 OCT 2006
 D QUE NOS L53
 D QUE NOS L54
 D QUE NOS L56
 L83 5 SEA ABB=ON PLU=ON (L53 OR L54 OR L56) NOT L77

FILE 'BIOSIS' ENTERED AT 13:51:18 ON 26 OCT 2006
 D QUE NOS L61
 D QUE NOS L62
 L84 3 SEA ABB=ON PLU=ON (L61 OR L62) NOT L78

FILE 'USPATFULL, USPAT2' ENTERED AT 13:51:21 ON 26 OCT 2006
 D QUE NOS L69
 D QUE NOS L71
 L85 3 SEA ABB=ON PLU=ON (L69 OR L71) NOT L79

FILE 'CAPLUS, MEDLINE, EMBASE, BIOSIS, USPATFULL' ENTERED AT 13:53:56 ON
 26 OCT 2006
 L86 22 DUP REM L81 L82 L83 L84 L85 (7 DUPLICATES REMOVED)

ANSWERS '1-15' FROM FILE CAPLUS
ANSWER '16' FROM FILE MEDLINE
ANSWERS '17-18' FROM FILE EMBASE
ANSWER '19' FROM FILE BIOSIS
ANSWERS '20-22' FROM FILE USPATFULL
D IBIB ABS HITIND HITSTR L86 1-15
D IALL L86 16-19
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FILE HOME

FILE CAPLUS

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FILE COVERS 1907 - 26 Oct 2006 VOL 145 ISS 18
FILE LAST UPDATED: 25 Oct 2006 (20061025/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

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FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 25 OCT 2006 HIGHEST RN 911284-77-0
DICTIONARY FILE UPDATES: 25 OCT 2006 HIGHEST RN 911284-77-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

FILE STNGUIDE

FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Oct 25, 2006 (20061025/UP).

FILE MEDLINE

FILE LAST UPDATED: 25 Oct 2006 (20061025/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
See also:

<http://www.nlm.nih.gov/mesh/>
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE EMBASE

FILE COVERS 1974 TO 26 Oct 2006 (20061026/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS

FILE COVERS 1969 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNS) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 18 October 2006 (20061018/ED)

FILE USPATFULL

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 26 Oct 2006 (20061026/PD)

FILE LAST UPDATED: 26 Oct 2006 (20061026/ED)

HIGHEST GRANTED PATENT NUMBER: US7127745

HIGHEST APPLICATION PUBLICATION NUMBER: US2006242744

CA INDEXING IS CURRENT THROUGH 24 Oct 2006 (20061024/UPCA)

ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 26 Oct 2006 (20061026/PD)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2006

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2006

FILE USPAT2

FILE COVERS 2001 TO PUBLICATION DATE: 26 Oct 2006 (20061026/PD)

FILE LAST UPDATED: 26 Oct 2006 (20061026/ED)

HIGHEST GRANTED PATENT NUMBER: US2006139723

HIGHEST APPLICATION PUBLICATION NUMBER: US2006242346

CA INDEXING IS CURRENT THROUGH 26 Oct 2006 (20061026/UPCA)

ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 26 Oct 2006 (20061026/PD)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2006

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